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Cardiac form of American Trypanosomiasis

by

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In the clinical picture of American Trypanosomiasis there are certain very constant and prominent symptoms which characterize the *cardiac form* of the disease. To give them firm foundation in fact and to avert the possibility of objections, our studies abound in decisive results derived from animal experimentation and human autopsies in which the constancy of the histopathologic processes and the presence of the parasites in the myocardium justify the interpretation of the principal features of the cardiac form.

In the clinical picture of this disease the lesions found in the cardiac muscle certainly represent the predominating factor; however, in a survey of the symptoms based on a large number of observed cases it is fitting to systematize the facts in two groups, one consisting of the cardiac changes of muscular origin and the other of changes associated with deficient nervous influences. These latter, which are attributable to the general pathologic processes of the disease, sometimes occur alone but usually are associated with changes of the former order. Here alterations of the cardiac rhythm occupy the chief place in the physical findings. Arrhythmia constitutes the predominant note in such cardiopathies, and in its various types are interpreted anomalies of the principal functions of the muscle. Furthermore, these types almost always succeed one another or complicate one another in the same individual. And this is not to be wondered at when one recognizes the progressive intensity and the diffusion of the pathologic process throughout the whole myocardium with its possible localizations in specialized functional zones of the organ.

For facility of description we must study the cardiac changes in the disease with the nature of the predominant arrhythmia. The functional changes of a general order, which give better ground for prognosis and so ought to form the criterion for a clinical classification, do not show appreciable variations but rather a relative uniformity in the different patients, and this prevents them serving for the basis of sharply delimited pathologic groups. Under these conditions we will study the following groups of alteration of rhythm:

1. Total tachycardias and bradycardias (of sinus origin)

2. Alterations of conductibility, manifested by

a. delay in the conduction of the contractile stimulus (increase of the space *ac* or P. V.)
b. partial block
c. total block (dissociation of auriculo-ventricular rhythm with persistence of ventricular rhythm)

3. Premature contractions:
a. auricular extrasystoles
b. ventricular extrasystoles
c. nodal extrasystoles

4. Auricular tachysystole (auricular flutter)

5. Paroxystic tachycardia (auricular, ventricular and nodal)

6. Complete arrhythmia (auricular fibrillation)

7. Cardiac alternations

These are the alterations of rhythm of which we have well-studied demonstrative examples. Some of them, of great frequence, indicate the affection of the organ in a very high percentage of the infected. This is true, in the first place, for the extrasystoles which are the most common of the changes of rhythm and constitute the best clinical symptom for the estimation of the endemic index of the disease. And the most frequent of the arrhythmias are those of conductibility, which among the many clinical features of trypanosomiasis represent that which is exclusively and peculiarly due to that disease. This is one of the great pathologic curiosities of the new disease entity, and in this chapter we find abundant valuable material for exemplifying and fundamenting the best theories of heart block, and for interpreting in the future, perhaps with greater certainty, the points that have remained open to discussion in this group of arrhythmias.

Other alterations of rhythm, associated like the two first with lesions of the muscle, are less common and we have only a few cases of them; in spite of this they are of value to characterize the sequence of the pathologic process and to better fundament the admitted pathogenesis. Among these are auricular tachycardia (auricular flutter) and auricular fibrillation. Why are they less common in this immense accumulation of morbid statistics with the most varied forms of arrhythmia? Why is the auricular fibrillation especially less common when in the opiniou of all the cardiopathologists it is the most frequent persistent irregularity of the human heart, represented perhaps by fifty per cent. of the clinical cases. We believe that in trypanosomiasis both are manifestations of the most advanced inflammatory processes of the myocardium and are the expression of a terminal condition rapidly followed by death. And, as a matter of fact, in the cases of this kind that we have observed up to the present time lethal termination occurred in a short time in the advanced conditions referred to.

Let us now see what are the appearances of the different forms of arrhythmia in the disease.

1. *Total tachycardias and bradycardias (sinus arrhythmia).* — The number of clinical cases of trypanosomiasis is high in which the cardiac rhythm is permanentlv accelerated or retarded, without the interference of accidental factors which could cause those anomalies. Usually these tachycardias and bradycardias are accompanied by extrasystoles of variable frequency; however, cases exist and are not rare in which protracted examinations do not show the presence of extrasystolic contractions, which are surely widely separated and even absent during long periods so that it is difficult to detect them. In this way the acceleration or slowing of the pulse with a regular succession of the pulsations predominates among the cardiac symptoms.

It must be emphasized that in such cases the auricles and ventricles pulsate at the same rate so that there is not here a sino-auriculo-ventricular dissociation.

How is the pathogenesis of these arrhythmias to be interpreted and how are their relations with the disease to be determined? Let us examine the clinical facts commencing with the tachycardias.

These tachycardias predominate in the female sex and there are a large number of patients in which the number of heart beats remains permanently between 100 and 200 or more per minute with regularity in the succession of the cycles or with the presence of extrasystoles. In these cases simultaneously with the acceleration of the heart beats there occur other symptoms which indicate the pathologic processes of the disease.

Furthermore, two large systems pertaining to the vegetative life, the thyroid and the genital, which play important parts in the physiologic equilibrium of the organism, show appreciable anomalies which are manifested by constant or very frequent syndromes in the patients of this group. The thyroid is almost always hypertrophied and the generative functions show marked changes which are expressed by intense dysmenorrhea with predominance of metrorrhagias. However, symptoms of hyperfunction of the ovaries constitute the principal genital syndrome, in which the considerable increase of the catamenias and the appearance of supernumerary menstrual periods characterize the functional derangement of the ovaries.

As regards the thyroid the facts are more complicated and the majority of the patients represent types of dysthyroidism with almost constant predominance of glandular hypofunction, but with isolated features of hyperthyroidism.

From this anomaly there must result physiopathologic consequences which are associated with either the function of one of the systems or with the disturbance of equilibrium in their interaction. Does the tachycardia observed constitute a part of such consequences? Aud does it indicate a hyperthyroidism? We must report that in men tachycardia is rarely observed although the anatomic alterations of the thyroid are of extreme frequency, and this indicates with all certainty the influence of the female genital apparatus in its mechanism. If the hypothesis of an endocrine influence on the chronotropic function of the heart muscle be admitted, and its importance even exaggerated, it would still remain to determine the exact process by which that influence is exercised in the cases we are discussing. Is there an increase in the tonus of the sympathetic attributable to the functional disturbance of the thyroid, and in consequence the acceleration of rhythm? But we must observe that in the cases of this kind, at least in the majority of them, there is found ovarian hyperfunction, manifested by its classical symptoms. Now, in accordance with the modern doctrines the ovarian hormone exerts a depressive action on the sympathetic, and this fact may contradict the interpretation just formulated. However, in spite of this, in the tachycardias observed we are enabled to exclude extracardiac interferences of a nervous nature associated with the endocrine processes. In the first place the sinus region can be attacked by the pathologic changes involving all the myocardium, and from this would result a greater excitability of the node of Keith and Flack. This by itself is capable of either causing the increase of the contractile stimulus (and in this case the tachycardia would be of intramuscular origiu) or of modifying too much the normal influence of the sympathetic, in this way occasioning the acceleration of the heart beats. Furthermore, and in the second place the possible interference of the suprarenal in these chronotropic changes must be admitted, since this is a frequent site of localizations of the parasite and of histologic changes, and its functional disturbance may act upon the cardiac rhythm.

And even this is not all of the difficulties in the interpretation that we are seeking, since those arrhythmias may be independent of extracardiac nervous factors and may indicate only the weakness of the muscle, thus representing the functional manifestation of the pathologic processes found there.

The complexity of the subject is evident and only protracted investigations can

later define the exact nature of the chronotropic disturbances in this disease, whose complicated pathology at times forms a decided obstacle to the interpretation of certain symptoms.

As regards the bradycardias of sinus origin we cannot escape the same lack of decision in attempting to interpret their mechanism. Do they indicate extracardiac influences in the form of deficient stimuli of the endocrine organs on the nervous apparatus that regulates the chronotropic function of the organ? Or do they rather indicate a disturbance of cardiac origin and manifest the weakness of the altered muscle? It should be emphasized that in these cases of bradycardia, as in the former case, the insufficiency of the organ becomes appreciable in all of its symptoms, which in a way may give a basis for the last hypothesis; far be it from us, however, to argue on this subject which should be reserved for later explanations. But we must refer to its predominance in males and this is an important factor to be considered in the necessary pathologic interpretation. Usually these bradycardias, as well as the tachycardias, are accompanied by extrasystolic contractions; cases exist, however, in which they constitute the only anomaly of rhythm.

The slowness of the pulse is very variable, oscillating in the vicinity of fifty beats per minute and is rarely seen below that figure.

Now let us pass to consider the arrhythmias that are indubitably related to the lesion of the myocardium. In the multiplicity of their varieties and in the frequence with which they are seen in nearly all of the clinical cases, these express a pathologic condition that belongs exclusively to this disease and they show the greatest curiosities in this new chapter of human pathology.

2. *Alterations of conductibility.* — The most curious and most characteristic aspect of the cardiac affection is that furnished by the alterations of conductibility, seen in all its phases of evolution from its slightest grades, which are manifest by simple delay in the conduction of the contractile stimulus from the node of Keith to the ventricle, up to complete block with independence of the sino-auricular and ventricular rhythms.

The number of clinical cases with this symptom that has already been verified is considerable, and we may say with all certainty that the knowledge of American trypanosomiasis in this particular has opened a new field in cardiac physiopathology with valuable indications, in which to the abundant concrete facts there is added the appreciable advantage of a known etiologic unity. In other diseases these alterations have been found; in none, however, with the frequency here recorded or with the manifold aspects and stages of development that can be encountered in trypanosomiasis. To such an extent is this true that we might characterize this entity as the disease *par excellence* of alterations of rhythm and especially of slow pulse.

We have found these alterations in all epochs in life, including even children of eight years of age, and here they do not constitute an appanage of advanced years, as is the rule, but depend exclusively upon lesions of the primitive cardiac bundles These regions are attacked by the diffuse pathologic processes characteristic of trypanosomiasis as much as the rest of the muscle; however, perhaps on account of their anatomic differentiation and greater functional importance there seems to be in these regions a preponderance of those processes which are manifest in the alterations of rhythm that we are discussing, and in others associated also with anomalies of the primitive bundles.

In the beginning the alteration is shown by the increase of the spaces *ac* and PR. which indicates the delay in the passage of the contractile wave through the normal paths of propagation. The increase of *ac* in many of our tracings reaches 0.6 and in rare cases has exceeded that time. The cardiogram and the radial tracing are sometimes regular; in the majority of the patient

however, the occurrence of extrasystoles comes in to complicate the arrhythmia and make the pulse irregular. In the jugular tracing the height of some or all waves constitutes a frequent anomaly and is attributable to the fusion of the ventricular wave of one cycle with the *a* wave of the following cycle. The number of cardiac pulsations depends on the sinus rate while the passage of the contractile waves is taking place and is not influenced by deficiency of conductibility.

In the next later phase of arrhythmia partial heart block appears, indicated at first by the periodic and spaced failure of transmission of some of the contractile waves and later by the greater frequency of the interrupted waves with establishment of a relation between the number of auricular and ventricular systoles (usually this relation varies between 3:1 and 2:1).

The immediate reason for the appearance of spaced failures of transmission of the systoles in the cases of increase of the space *ac* is variable and could only be appreciated by an analysis of the tracings. Often those failures indicate exclusively the exhaustion of the conductibility and no other factor is of influence; frequently, however, the gradual delay in the transmission of the systoles, causing the delay of the refractory phase of the ventricle, renders ineffective contractile waves which otherwise would be effective and could complete the cardiac cycle. And still other factors may intervene here. The same reasoning is applicable to the most frequent alternation of the relation of 3:1 to that of 2:1, or vice versa, and only concrete cases lend themselves to explanations in this way.

The last stage of these chronotropic alterations is that of complete block with a permanent idioventricular rhythm. We already have a large number of cases of this group, all more or less uniform in their clinical manifestation and in the course of their symptoms. When one considers the etiologic unity of the syndrome and takes into account the short space of time that has sufficed for us to collect so large a number of observations in a scattered population, the high scientific interest of this chapter of cardiac pathology becomes abundantly evident.

The number of radial pulsations in cases of complete block oscillates in the vicinity of thirty and sometimes reaches, but rarely exceeds, forty. We have seen a rate below the first figure in some patients, almost always on taking more or less fatiguing exercise. And the progressive diminution of the pulsations to five per minute was observed in one case of death from exhaustion of conductibility.

In some patients it has been possible to accompany the progressive evolution of the arrhythmia from its commencement, with at first only a delay in the conduction, followed by the periodic and rare failures in the passage of the wave, and then the establishment of a fixed relation between the complete cardiac cycles and the blockades, and finally the complete block and consequent presence of the true ventricular rhythm. It must be noted that this last condition is the most persistent and the others represent in this disease only transitory passing phases of the ever advancing process. Some of our patients with complete block have survived the arrhythmia for a considerable period of time; in the majority of them, however, death has occurred as the result of the affection.

Among the most notable characteristics of the tracings in these cases is the frequent irregularity due to the presence of extrasystoles. And, indeed, the heterogenetic pulsations of ventricular origin form a symptom frequently preceding the disturbances of contractibility, which indicates previous changes of the whole muscle or of the primitive bundles scattered through it and localized later in the conducting regions. The simultaneous tracings of the jugular pulse, heart beat and radial pulse show here variations, all occurring more or less along the

general lines already known in similar cases of whatever etiology. Only the study of the concrete facts could furnish interesting pathognomonic data. Other subjective and objective symptoms of the cases of block are of great value; however, let us reserve them for later explanation and pass now to the study of the extrasystoles.

3. *Extrasystoles.* — The function of excitability is attacked in the majority or perhaps in all of the chronic cases of American trypanosomiasis. The patients with extrasystoles are almost counted by the number of infected, and such is the frequency of the symptom that we use it with profit as the best factor for estimating the endemic index of the disease.

Extrasystolic contractions are seen from the least advanced ages to old age and the number of children in whom we have found this alteration is quite high, and this is also a condition peculiar to trypanosomiasis. However, they are not found in the acute cases of the disease in spite of the intense lesions of the myocardium in the initial phases of the infection when the parasites are found in great abundance in the heart muscle.

It is clear from this that the extrasystole indicates rather a process of diffuse myocarditis and is more closely related to fibrous changes in the muscle than to the acute inflammation that is found in the early stage. As regards its origin these heterogenetic pulsations can be referred to the ventricle, to the auricle and to Tawara's node; here, however, as is general for this symptom, the ventricular extrasystoles predominate and are observed in a very high percentage relatively to the others. The auricular extrasystoles are somewhat rare, also those of nodal origin.

The inconstancy of the symptom in some cases should be emphasized, and this often makes its observation difficult and may lead to wrong conclusions from its absence. Some factors, whose intervention must be profited by in doubtful cases, especially influence its appearance. In the first place is the attitude; the extrasystoles are frequent principally in the dorsal decubitus, and many patients who show regularity of the pulse in the vertical position present extrasystolic contractions when lying down. Next come effort, fatigue and emotion. Often we only succeed in finding the symptom by causing forced movements of the patient or by producing sudden emotions. And in spite of the interference of the factors referred to the individuals are not rare in whom the extrasystoles are periodic, and only appear from time to time, with intervening phases of regular rhythm.

The frequency of the symptom in different patients or in different phases of the same case is very variable. Sometimes the extrasystoles are separated and only appear at long intervals in the tracings; others, however, present themselves with great frequency, being repeated in every cardiac cycle or two in the same cycle, giving the tracings the classic appearance of bigeminism and trigeminism.

It is of greater importance to note the prolonged sequence of extrasystoles with absence of compensating rest between the interposed beats, present in the beginning and end of the group, aud this is characteristic of the crises of symptomatic paroxysmal tachycardia in this disease. We have various observations of this symptom which show the occurrence of the attack at the moment when we were taking the tracings; however, it is possible to judge of its frequence from the histories given by the patients with extrasystoles, who, as a rule, refer to transient crises of palpitation with rapid beating of the pulse and appreciable and very inconvenient contractions of the heart.

Taking into consideration the moment of the diastolic phase of the cycle in which the extrasystolic contraction appears, we must emphasize here the presence of interpolated extrasystoles in many cases. Relatively rare in the alterations of excitability

in general, these are here somewhat common, indicating the exaggerated irritability of the heart muscle. No common description of the tracings of extrasystoles would be possible, and in each one of them we find various factors which show the extreme variability of this symptom and its frequent association with other alterations of rhythm. We here show some very demonstrative analyses of tracings.

The subjective symptoms that occur in the course of this alteration of rhythm, or consequent upon it, are of decided interest aud will be referred to in the followiug paragraphs.

4. *Auricular flutter.* The alterations of rhythm manifested by auricular flutter and auricular fibrillation are among the rarer observations, but are of the highest scientific interest. We have various cases with alterations of this nature and in them the essential characteristics of these forms of arrhythmia are well shown. Auricular flutter has been observed in various degrees of intensity with the number of auricular contractions varying between one hundred seventy and five hundred per minute. This last figure is one of the highest yet registered in the medical literature and was seen in a case that soon passed to the condition of complete arrhythmia. The number of auricular waves transmitted to the ventricle has always been variable in the different patients that we have observed, and no fixed relation has existed between the rhythm of the auricle and that of the ventricle within the limits of the tracings. This has given rise to irregularity of the radial pulse and this fact also shows the high grade of heart block of the cases of flutter in this disease.

Extrasystoles are also a somewhat frequent simultaneous occurrence in the cases that we are discussing, and their presence also gives rise to a greater irregularity of the cardiograms and of the radial pulse.

Some of our patients exemplify the transition from flutter to auricular fibrillation, and other cases show intermediate phases between the two alterations of rhythm.

6. *Complete arrhythmia.* The observations collected on complete arrhythmia have been relatively small in number considering the high incidence of changes of the heart rhythm in this disease. The cases investigated occur in more or less the classic condition of this syndrome, as can be seen from a study of the tracings. We see ventricular venous pulse with waves of variable appearance, complete irregularity of the radial pulse and of the cardiogram, and it is sometimes possible to see in the jugular tracing small undulations which indicates the fibrillar state of the auricle.

The two last forms of alterations of rhythm without doubt express the greatest intensity of the pathologic processes of the myocardium in the disease, and also indicate localisations of those processes in the auricles, whose irritability becomes thus manifestly augmented even up to absolute inefficiency of the respective systolic movements.

From the beginning the affection of the myocardium is most intense in the ventricles as is well manifested by the extrasystoles originating in these regions. And when the alterations of rhythm indicate marked lesions of the auricles the prognosis becomes grave, as is shown by the termination in death within a short time of all our cases with auricular flutter and fibrillation. And, on the other hand, we must emphasize the relative scarcity of observations of these two arrhythmias, a fact which is evidently at variance with the constant intense lesions of the heart muscle and with the great number of other alterations of rhythm. On the best of grounds we believe that the rarity of these arrhythmias is only apparent as they are difficult to be detected in clinical investigations on account of the extreme gravity of their prognosis. The patients affected with them survive only a short time or remain in extremely serious condition; and as they are kept to their houses they escape the oppor-

tunity of medical observation, under the conditions under which our work was done. Another interesting thing with regard to the cases of auricular fibrillation is the absence of valvular lesions, since these lesions, especially of the mitral, are the most prominent features in the present medical literature on this chapter of cardiopathology.

7. *Alternation.* Alternating pulse figures in many of our observations accompanying various of the arrhythmias referred to. Its greatest frequence is observed in the cases of extrasystoles where it characterizes the post-extrasystolic alternation and where it almost always represents a transitory condition, disappearing after a few cycles of dominant rhythm.

The alternation is rarely observed as an isolated symptom, and from what we have observed we cannot estabish a relation, in the cardiac form of the disease, between this symptom and any certain prognosis of great gravity.

General symptomatology of the cardiac form.

Although extremely variable in the different patients the clinical symptoms of the affection of the myocardium in trypanosomiasis can be considered in a joint description, leaving aside the details and using only the principal facts or, rather, those that are repeated with the greatest frequency in the manifestation of the cardiac form.

The symptoms of insufficiency of the organ occupy the first place and are indicated by their usual features: low arterial tension, visceral congestion, dyspnea, fatigue on exertion, edemas, etc., all expressing the progressive exhaustion of the heart's activity. Of these symptoms the edema deserves special mention as regards its appearance.

Even in the cases of most intense affection of the myocardium we rarely find here the extensive infiltrations seen in Bright's disease. The edemas in these cases are relatively slight, doubtless on account of the absence of renal changes, and on account of this and the intense toxic conditions the origin of the infiltration in this disease is essentially limited to the weakness of the heart muscle. The great generalized infiltration is only observed in some relatively rare cases of cardiac asystole. And even at the time of the death agony with progessive weakening of the myocardium the edema is not present to the extent of that of renal origin.

As a physical sign of great frequency we must refer to the increase in volume of the heart. This sign is observed in any of the groups of the arrhythmias referred to, and sometimes indicates the hypertrophy of the muscle and at others the dilatation of its cavities or the two conditions simultaneously. We must also refer to other cardiac signs, such as the murmurs of relative valvular insufficiency, the obscuring of the heart sounds, especially of the first sound, the alterations in intensity and amplitude of the apex beat, etc..

Other cardiac and circulatory physical signs occur with frequency and ought to merit attention. But let us consider some of the more characteristic subjective symptoms, especially those directly related to the different forms of arrhythmia or, better, to the lesions of the myocardium.

Avexame (anxiety, agony, *angor animi*). This is the expression by which the patients characterize subjective phenomena, doubtless of circulatory origin, which figure in the history of numerous clinical cases whatever be the form of the arrhythmia. There is no uniformity in the facts included under this denomination, and it would therefore not be possible to refer them to a single origin. The patients indicate in various ways the subjective phenomena that they suffer which constitute the "agony." Some complain of precordial anxiety, of a sense of constriction originating in the epigastrium or the precordium and ascending to the throat, where it is most intense and causes phenomena of dyspnea and oppression frequently followed by fainting and

transitory dizziness. Others refer to a condition of general *malaise*, with unpleasant perception of the heart beats, rapid or slow, and painful sensations in the epigastrium and larynx accompanied by respiratory difficulty, etc. Finally, a large number of patients only complain of the "agony" without being able to define or localize the sensations that constitute it.

In any case, what is the exact pathognomonic value of this expression? Must we find a relation between it and some definite cardiac mechanism, and so find its true pathologic interpretation? Certainly not. "Agony" means nothing to the student of symptomatology but everything to the patient. This word includes the most varied sensations, all of circulatory origin but without the uniformity necessary for including them in a joint definition. No doubt can exist with regard to the relations between such phenomena and the processes of myocarditis and tho various forms of arrhythmia of the disease. The «agony» is no nosologic novelty; it only reproduces here on a large scale subjective symptoms that are well known in cardiopathology and are associated with the different cardiac arrhythmias.

In this disease those sensations are often related to the extrasystoles and indicate the circulatory results of the compensatory pause, either alone or associated with an unpleasant perception of the extrasystolic beating. They may further be due to the crises of symptomatic tachycardia, to the alterations of conductibility, and to the other arrhythmias observed. And even this is not all of the pathologic conditions of "agony", that is, of the more or less painful sensations referred to by the patient. We believe in the interference of lesions of the intracardiac sensory nerves and are planning investigations to clear up this point. And, furthermore, we must add that "agony", or the sensations that correspond to it, is often complained of in the absence of appreciable arrhythmias.

Palpitations form another symptom of great frequence in the cardiac form of the disease. They occur almost always in crises of short duration, appearing and disappearing suddenly, and they subject the patient to the most painful sensations. The palpitations are not always related to the accelerated rhythm of the heart; often they appear with a normal or even diminished number of heart beats and radial pulsations. This symptom expresses the unpleasant perception of the heart beats, and for this very reason is not related to the various types of arrhythmia but to the anatomic processes that determine them. The palpitations in the patients that we have observed come on without any determining cause, when they are in repose or in motion, excited by slight exertion or by sudden emotions. They also disappear without any immediate cause.

The characterization of the symptomatic paroxystic tachycardia is clear, and is so much the more admissible since it has been possible in some crises of tachycardia to detect in the tracings the beginning or the end by an extrasystole.

Faintness forms another symptom of great frequency, complained of in various degrees, sometimes limited to simple transitory obscurity of vision and at other times more intense and accompained by vertigo with loss of consciousness. In any of the forms of arrhythmia this symptom is observed, but its greatest frequency is related to the circulatory changes caused by extrasystole. In addition to the faintness syncopal and convulsive attacks occur as nervous symptoms of the cardiac form. These may be observed in various of the arrhythmias, indicating the deficiency of irrigation of the nervous centers caused by the arrhythmia. However, such symptoms are better characterized in the alterations of conductibility and here complete the Stokes-Adams syndrome.

In the patients with heart block the nervous symptoms are very frequent in any

of the phases of the arrhythmia, in the earliest as well as in complete block. And here, with the great number of cases that we have, we cannot confirm th greater intensity of such symptoms in the phases that precede the establishment of the idio-ventricular rhythm. Vertigo, syncopal attacks and convulsions have been seen in patients with partial and total block, perhaps in a little larger number of the first but in all stages of the arrhythmia.

At this point it should be noted that the number of ventricular beats in cases of complete block undergoes frequent variations, which arë doubtless related to the alterations in excitability of the muscle. From forty pulsations to the minute, and sometimes more, the rate of the idio-ventricular rhythm passes to thirty or even less, and this may explain the frequency of nervous symptoms in cases of this kind.

Other symptoms could be given here if we wished to glean them from the great number of observations of the cardiac form that we have. We prefer, however, to at once treat of other subjects.

Course.

As regards the clinical course of the cardiac form we must state that this is the type of the disease that occasions the greatest mortality.

The death rate in the cardiac form is relatively very high; in spite of this, a large number of cases remain in a state of tolerance for many years, capable of carrying on their work, although the insufficiency of the heart is more or less marked. According to our observations, this can be found in nearly all forms of arrhythmia except those of flutter and auricular fibrillation, the prognosis of which we consider very grave and we do not believe that thev can long survive. In a general way we can state that the course of the cardiac affection in this disease is progressive. Here there is no possibility of regression and the patients proceed more or less rapidly to a lethal termination.

Death from the disease.

SUDDEN DEATH

Sudden death is extremely frequent in the regions of endemic trypanosomiasis. We have had the opportunity of seeing it in several cases of the cardiac form at the place where we were carrying on our work and its frequence is made more impressive by the unanimous reports of the inhabitants of such regions where a large number of the families mourn the sudden death of one or of various members. The individuals frequently die in the fulness of their youth and in an apparent healthy condition during the phase of tolerance of the cardiac affection. Many of them die while engaged in their usual work without any immediate cause to explain the occurrence; but others die at the moment of an extra exertion, or of fatigue, or of some other accident that is capable of exhausting the deficient energy of the myocardium. Facts of this kind are numerous and plainly show the intensity of the pathologic processes of the disease. We do not know of another condition in human pathology that causes sudden death in so high a proportion of cases as does American trypanosomiasis.

What is the exact mechanism of this death? Can we determine it with certainty in a way to cover all of the facts? And will it be the same for all of the occurrences of this order? In the explanation of this mechanism we must note in the first place that sudden death is observed in any of the forms of arrhythmia, which in a way renders its exact interpretation difficult. On the other hand we must remember that usually the patients show different forms of arrhythmia simultaneouslv and that cases are rare that have one form of rhythm exclusively. And if this is so, the unity of that mechanism must be admitted once there is recognized the occurrence of the fact in one of the most frequent arrhythmias. Now, of these, arrhythmia by extrasystole is doubtless that which is repeated in the greatest number of patients associated with other

forms of alterations of rhythm. Can sudden death in the disease depend upon the extrasystoles and upon these exclusively? We must remember that the compensatory pauses of the extrasystolic contractions and their inefficiency in the propulsion of the blood certainly cause profound circulatory embarrassment that frequently determines the occurrence of faintness, vertigo, loss of consciousuess and syncopal attacks, etc. In this disease, as our accumulated mass of observations on the heart amply demonstrate, the alterations of excitability of the myocardium are profound, and as a result extrasystoles occur sometimes very frequently, repeated two or three times in the same cardiac cycle. Hence in many cases profound circulatory alterations intervene in the nervous centers of the myocardium itself, and these may explain the sudden death. This is an hypothesis.

There at once occurs to us another hypothesis, also based on fact and perhaps more in accordance with cardiac physiopathology. Auricular fibrillation has been found in this disease and we believe if is not a rare process although relatively less frequent. While limited to the auricle this alteration does not impede the circulatory efficiency; but propagated to the ventricle, as it may be, there soon occurs a failure of the circulation and as a direct consequence rapid death. Is this true in the cardiac form?

Let us discuss it briefly. The frequence of ventricular extrasystoles and their repetition two or three times in the same cycle express an irritability of the ventricular myocardium, a condition very near to that produced experimentally and indicated by a fibrillar state of the muscle. One degree further in the pathologic process and the excitability of the ventricle will perhaps reach a condition similar to that of the auricle, with the terminal failure of the rhythm. Moreover, we have the opportunity to exhibit tracings in which the ventricular extrasystoles, up to seven in number and all abortive, are repeated in the same cardiac cycle. The extrasystolic contractions here are so weak that they look like simple tremors of the muscle and are completely useless in the circulatory mechanism.

We must at once refer to MacWilliam's hypothesis which has formed the basis for our argument and in which sudden death in intense disorders of rhythm would be explicable by fibrillation of the ventricle.

DEATH IN AGONY (MORTE AGONICA)

Here with greater frequence the essential fact is the progressive insufficiency of the myocardium from which asystole results. This insufficiency is principally of cardiac origin, and the renal apparatus, whose functions are little if any affected in this disease, does not particate in its occurrence. In this way the greater number of patients of the cardiac form die, in acute or chronic asystole, from rapid dilatation of the ventricles, and others die from progressive exhaustion of the muscle.

Another aspect of death in agony is observed by the diminution of the idio-ventricular beats, with long diastolic pauses. We have observed one case of this kind in which the ventricular rhythm fell slowly to the minimum of five pulsations per minute or with diastolic pauses of twelve seconds.

These are the commonest conditions of death in the cardiac form.

We have only considered the facts of greatest frequence and have left aside other occurrences such as fatal accidents in children with symptomatic tachycardia, deficiencies of conductibility with partial block, profound alterations of contractibility, etc. Death may here result from various conditions aside from those most frequent ones, as is not difficult to understand when we know the intense lesions that attack the muscle.

Influence of atropine on the alterations of cardiac rhythm in the disease.

The results of the experiments performed by one of us relative to the action of

atropine on the arrhythmias of the disease have been very interesting. As the result of a large number of cases we have concluded that the dromotropic action of that remedy is very marked and that its habitual chronotropic action is very small and even unappreciable in many cases. Here in some way there occurs the physiologic dissociation of the fibers of the vagus, and the atropine acts predominantly on those that interfere in the conductibility of the cardiac muscle.

Several cases of complete block, others of partial block and many of extrasystoles were the subject of the experiment.

In complete block the dromotropic action of the remedy was nil and the independence between the sino-auricular and ventricular rhythms remained unaltered. In the same cases the chronotropic action made itself felt very slightly, and often in a negative sense, that is, by causing the paradoxical effect of diminishing the number of beats of the auricle.

The experiments relative to partial block were of greater interest. In this case the elective action of the atropine on the conductibility was notable. In the majority of the experimented cases the remedy regulated the rhythm, that is, normalized the deficient conduction. The chronotropic action was unappreciable or at times acted in a negative sense, diminishing the number of auricular beats.

How is the restoration of conduction by atropine in the cases of heart block to be interpreted? Must the nervous origin of the alterations of conductibility be admitted here? No. The muscular nature of such alterations is clear and is demonstrated by the direct proof of the lesions of the myocardium. Furthermore, the cases of complete block, which represent only a more advanced degree of arrhythmia and whose pathogenesis is identical to theirs, was not modified by the action of the atropine, which excludes the entirely nervous nature of the disturbance of rhythm.

No doubt could exist about the only possible interpretation of these results. The lesions of His' bundle make it more excitable and give rise to the increase of physiologic tone of the vagus with the consequent alterations of conductibility that can be corrected by atropine, If these lesions were more intense, the atropine would not act in the same way, for there the block is already independent of the nervous action and is associated exclusively with the pathologic process of the muscle.

Moreover, the influence of anatomic changes of the conducting bundle on the inhibiting effects of the vagus is demonstrated in the experiments on the action of digitalis, although in a sense antagonistic to that referred to the action of atropine.

According to Mackenzie, digitalis exerts no action on the conductibility of normal beats, but with the presence of lesions of the muscle that remedy, even in a therapeutic dose, increases the time of conduction of the sinus stimulus to the ventricle, eventually producing partial block. We know of no case reported of total digitalis block in man, and therefore the importance of one of our cases increases in which the action of crystallized digitalin determined the appearance of a total block with the nervous symptoms of the syndrome. When the use of the remedy was suspended, the total block was transformed into a partial one, and the radial pulse rose from 35 to 50. Simultaneously the nervous symptoms disappeared and other symptoms associated with the block diminished. However, in this case the action of the digitalis caused a considerable increase of the vagus tonus on the injured His' bundle. When the use of the remedy was stopped, the altered dromotropic function returned to its former condition.

It is, without doubt, less easy to interpret the paradoxical effect of the atropine on the chronotropic function, especially appreciable in the cases of partial block. Similar facts are reported in the medical literature in cases of alteration of heart rhythm; but

in these cases there is a lack of acceptable interpretatious, nor do we possess any facts that can serve as a basis for hypotheses that can explain that phenomenon.

Although our experiments were performed on a large number of cases, we can state nothing decisive in regard to the influence of atropine on the extrasystoles. We can state nothing from the occurrence of negative cases which indicate the absence of any action of the remedy beside others in which the rhythm was regulated. Furthermore, the inconstancy of extrasystolic beats is well known, as they often disappear for long periods even in clinical cases in which their frequence is greatest.

Allorhythmias.

In the tracings of the cardiac form of the disease we have found anomalies of rhythm that are repeated regularly and periodically, thus giving uniform appearances which can be grouped under the denomination of allorhythmias. Various factors enter into their origin and hence the principal interest is trying to recognize the conditions that determine them.

The most characteristic of such appearances are the bigeminism and trigeminism that may result in the same case or in different cases from differences of cardiac rhythm, isolated or combined.

The bigeminism usually results from extrasystoles which are repeated in all the cardiac cycles and the trigeminism from two extrasystolic contractions; further, both the appearances may depend upon alterations of conductibility or upon these associated with extrasystolic contractions. Only the analysis of each tracing in concrete cases can determine the relations between the allorhythmia and the facts that cause it.

Aside from these we have met other appearances of allorhythmia in which the irregularities are periodic and asssociated with different conditions, such as auricular fibrillation, and the interposition of extrasystoles which succeed one another regularly. Such facts are exemplified in some of our tracings and their semiology can there easily be seen.

The cardiac form of the disease being thus described in its essential outlines, the interest of this new chapter of human pathology is evident and the great pathologic curiosity of the new trypanosomiasis in this clinical phase becomes apparent. It is clear that the subject is far from being exhausted in this first summary description of the cardiac form; there is much here for further investigation in the interpretation of the symptoms and for an exact knowledge of other cardiac conditions of the disease.

Aside from the present clinical observations the description here written is based on the works of pathologic anatomy and histology begun by the lamented Gaspar Vianna and completed by our eminent friend Professor Bowman C. Crowell and our companion Magarinos Torres.

The clinical observations that have been presented represent a small, selected, number of the large group of cases that have been studied. However, by the uniformity of the cardiac syrdrome made manifest by them, they show the etiologic nnity of the morbid process localized in the cardiac muscle.

This condition of the disease, in which cardiac symptoms predominate over all others, is generalized in the zones of endemic trypanosomiasis, and it is there observed with a maximum intensity and extension, thus forming the clinical characteristic *par excellence* of the American trypanosomiasis.

The certainty of the etiology of all the clinical obsevations here presented cannot be contested, although in many of the patients neither the parasitologic diagnosis nor the necroscopic proof has been made.

In the cases in which necropsy was possible, already a considerable number, the symptomatology was well studied and was in every point identical to those here reported. This assures with absolute certainty and irrefutable scientific precision the etio-

logy and pathogenesis of the numerous clinical cases of the cardiac form that we possess. Furthermore, the localization of the parasite in the heart muscle is a constant occurrence in the infections by tle *Trypanosoma cruzi* not only in man but also in laboratory animals as well.

On the other hand the more recent histopathologic studies of Dr. Crowell show lesions that are considered by him as characteristic of the action of the parasite on the myocardum in the chronic process.

It may also be stated that the studies of Dr. Crowell have shown well localized lesions in the primitive cardiac bundle, which explains the anomalies of rhythm shown by the physical examination.

Observation no. 1.

Cardiac insufficiency. Total bradycardia. Sinus arrhythmia.

J. P.—White, 21 years, male, laborer, single, resident at Santo Antonio da Lagôa.

The patient has always been strong and mentions no former ailments. For the last few months he has a feeling of fatigue and gets tired after exertion. He came however to consult us on account of nocturnal delirium. In appearance the patient is strong, muscular and well built. There are no subjective signs to be noticed. Cardiac area enlarged, apex beat in the 5th intercostal space, outside the mamillary line. Heart sounds quite audible, no murmurs. Pulse arrhythmic, the beats now slow, now fast, at times simulating extrasystolic beats. Number of beats per minute: lying down 50; standing 82. Tmx.=140. Liver slightly enlarged. Spleen not enlarged. Cervical and inguinal glands slightly enlarged. Thyroid gland hypertrophied.

Record no. 1.

The radial and cardiac tracings show that between the first and fourth cycle the interval diminishes; the diastolic pause lengthens suddenly from the fourth to the fifth cycle and diminishes again gradually until the seventh. At the seventh the same succession of sudden lengthening of the diastolic phase with gradual shortening every four beats begins anew. The long diastoles are however not strictly equal nor are the short ones so that the pulse is very arrhythmic. The amplitude of the pulse wave is in proportion to the length of the preceding interval. On analysis, the venous tracing shows the same irregularity in the succession of the auricular waves; it is the auricular rhythm which is altered in the first instance. The *a c* interval remains normal and there is no change in the conductibility. The regular succession of long and short diastolic phases every four beats shows that the arrhythmia is of respiratory origin, although the curve does not register the oscillations of the respiratory rhythm. The pulse is that found in total bradycardia, 50 beats per minute.

Observation no. 2.

Total bradycardia. Spasm of the esophagus.

A. S., negro, 23 years, male, single, resident at Santo Hipolyto, near Lassance. Examined June 23, 1916. The patient came to the hospital on account of an *entalo* (spasm of the esophagus) which he has had for four years and which started after a fever which lasted about fifteen days. The patient has difficulty in swallowing both liquid and solid food; it "goes down with difficulty and stops in the throat"; the patient finds deglutition painful and often has spasms of pain after it. Sometimes while swallowing the food is regurgitated. The difficulty is not continuous, but rather periodic and irregular. At times the patient swallows both liquid and solid food easily, at others, he has to take a draught of water after each particle so as to be able to swallow it, and, at others he cannot swallow even water. Certain foodstuffs, such as beans and peppered food, seem to bring on the spasm whilst farinaceous ones do not. The pa-

tient retains his appetite, but feels burning in the stomach, which is allayed by draughts of cold water. For about a year now, he gets easily tired and has palpitation after making any effort. The patient also mentions a feeling of weakness and pains in the legs, and slight vague pains in the body. At times, when obliged to drink much water so as to swallow, he vomits his food.

The only former ailments the patient mentions are attacks of fever, the first of which appeared six years ago and the last about two months ago.

The patient is well built and strong looking. On both sides of the parotid region, there are soft masses about the size of almonds, which seem to be due to a hypertrophy of the parotid glands. The patient states that their size varies, increasing at times and diminishing at others. Heart not enlarged; apex beat 7.5 cm. from the midsternal line, the right margin 3 cm. from the same line. Heart sounds clear. The second sound increased and reduplicated at the pulmonary area. Pulse slow, 44 lying down and 52 standing, accompanying the heart beats. After slight exercise, 70. Katzenstein test positive; Tmn.=75. Tmx.=115.

Liver not enlarged, not painful on pressure. Thyroid gland enlarged, with a cyst about the size of a walnut in the middle, and smaller local ones. Inguinal glands slightly enlarged. Nervous system negative. Intelligence of a low order.

An X—ray examination of the process of swallowing was made. A bismuth emulsion was easily swallowed, but corn mush containing bismuth was swallowed very slowly and stopped several times owing to a spasm of the esophagus, provoking a feeling of discomfort and pain. The spasm was stronger at the cardia; as the patient put it "the stomach does not want to let food in".

Record no. 2 and 2-A

1) Pulse as in total bradycardia, as may be seen by the jugular and venous tracings. The *a c* interval not lengthened; the dominant rhythm regulated by the auricular waves. The venous tracing shows the *b* waves of Hirschfelder well. Sudden pressure on the eye-balls produces a stoppage of the pulse for 4:5 seconds.

II) It is also a total bradycardia tracing like the former one and shows the effect of slow ocular pressure. The pulse has become much slower and the retarding influence seems to make itself felt after the pressure has stopped. It is interesting to note that after the compression has ceased the ventricle goes on beating with its own idio-ventricular rhythm. independently of the auricular rhythm, which is slower and the waves of which make themselves felt at the systolic ventricular phase by very acute rises.

The auricular beats gain in speed gradually until they dominate the rhythm. The last beat in the tracing belongs to the auricular rhythm. The last but one shows a fusion of the *a* and *c* waves.

This shows that though the diminution of excitability produced by ocular compression acts on all the points of origin of the cardiac contractions, it has a much stronger influence on the sino-auricular ones than on the starting-points of the idio-ventricular rhythm.

Observation no. 3.

Simple tachycardia.

G. do N., negress, 30 years resident at Lassance.

Examined at

Previous history of no special importance; the patient states that she has always been well, and has had no disturbances other than those which go with gestation. She has three children one of which was born prematurely at seven months. She has been ill for three months with loss of appetite and a feeling of fulness in the stomach after even moderate eating; poor digestion. Is easily fatigued and has "avexame", agony in the heart and a feeling of

anguish. Palpitation with rapid beats, which condition sometimes lasts an hour and is accompanied by a feeling of agony ("avexame").

Record no. 3 and 3-A.

Taken at a crisis of palpitation. The tracing is perfectly regular only the rhythm is accelerated, 120 beats per minute. We were unable to follow the transition between this and the slower thythm of 3 which accompanied the disappearance of the subjective sensation of palpitation and agony. Nor can we affirm whether the greater rate was brought on by auricular extrasystoles or by the simple acceleration of the normal rhythm.

Observation no. 4.

Tachycardia. Palpitation.

F. P., negro, male, 25 years, resident at Lassance.

The patient came to be treated on account of strong and uncomfortable heart beats and agony ("avexame"), and states that he often gets frightened without any reason. This condition is accompanied by palpitation and agony ("avexame") and causes him much discomfort; it has lasted for over a year.

Signs of slight cardiac insufficiency, The heart is not enlarged. Heart sounds clear, without murmurs, Thyroid enlarged, with moderate sized goiter. During palpitation the heart beats are frequent and violent so as to shake the thoracic wall; the respiratory movements are more frequent and the breathing anguished. There are no lapses of the pulse either at the time of the palpitation or in the intervals.

The tracing shows an extrasystole at the end of an attack of palpitation.

Record no. 4.

Taken at the final phase of an attack of palpitation. A ventricular extrasystole is shown, but it was not possible to take tracings showing the real nature of the acme beats during palpitation.

Observation no. 5.

Asystole.

R. M., white, male, 17 years, resident near Lassance.

The patient suffers from palpitation, is easily fatigued and has attacks of dizziness almost always followed bv fainting. He has become thin. No edema. Signs of cardiac insufficiency. Pulse arrhythmic, at times with heart beats in bigeminal and trigeminal groups. Heart beats 84, which is more than that of the radial pulse, 73, because not all the extrasystoles are shown in the pulse. Tmx.=105. Thyroid gland hypertrophied, specially the middle lobe. Many cervical glands.

This patient was put in hospital during a crisis of cardiac asystole. At the time there was generalised edema with intense dyspnea and visceral congestion. The patient died of cardiac collapse. The histopathologic examination made by Prof. CROWELL showed parasitic foci and intense lesions of the myocardium.

Observation no. 6.

Ventricuiar extrasystole. Cardiac insufficiency. Palpitation. Agony.

M. A., mulatto, 23 years, female, married, resident at Pirapora.

Previous history of attacks of intermittent fever, and a little while ago arthritis of the wrist after a gonococcic infection which was cured. For some time the patient has been feeling nervous excitability, palpitation and fatigue on exertion. Nocturnal dyspnea with palpitations. These symptoms have become more pronounced in the last fifteen days; she has also gastric pains, a feeling of sickness and abundant salivation. Palpitation with agony ("*avexame*") almost constant.

Precordial beats very violent, with very marked apex shock. Cardiac erectism. Apex

beat in the 4th intercostal space, 7.5 cm. from the midsternal line; right margin 3.5 cm. from the midsternal line; no increase of the cardiac area. First sound muffled; second reduplicated, with pulmonary accentuation. No murmurs. Pulse very visible in the veins of the neck. Pulse full and unstable, accelerated on any emotion. Extrasystolic arrhythmia. Number of pulsations varying from 96 to 85 when lying down, the extrasystoles being more numerous when the pulse is more rapid. Standing, the number of pulsations rises to 100 and after slight exercise to 108. Tmx=140.

Liver not enlarged. Spleen slightly enlarged. Thyroid enlarged, with slight exophthalmus. Peripheral glands not enlarged. Menstruation regular, generally accompanied by slight pains. There are signs of double ovaritis.

July 15, 1913. General condition without noticeable change; but the indefinite malaise, agony and following palpitation continue. 88 beats per minute. Tmx=130.

Record no. 5.

The radial tracing shows that extrasystoles interrupt the dominant rhythm frequently and that the latter is also variable; the *a* waves not being perfectly rhythmic. On the right side of the tracing the arrhythmia of the *a* waves and of the pnlse are accentuated by the movements of deglutition; acceleration at the moment of swallowing and subsequent retardation.

The extrasystoles are ventricular with complete compensating period. This tracing was taken at a time when the patient complained of palpitation with strong feeling of agony ("*avexame*".)

Observation no. 7.

Ventricular extrasystole.

E. A., Syrian, 20 years, male, single, resident at Lassance for the last two years.

Examined July 20, 1910.

The patient is a native of Syria and has been in Brasil for two years. About three weeks before being examined he noticed that his thyroid had become enlarged and felt uncomfortable. There were no other morbid phenomena, or fever.

Pulse regular, 64; the rhythm interrupted by extrasystoles. Slight signs of cardiac insufficiency, with positive Katzenstein test.

Record no 6.

The rhythm of the radial tracing interrupted by a feeble extrasystolic beat which according to the analyses of the jugular tracing seemed to be an interpolated extrasystole (marked *c*).

Observation no. 8.

Interpolated ventricular extrasystoles.

E. A., resident at Santa-Maria.

April 2, 1911.

Large goiter. Liver enlarged. Signs of cardiac insufficiency. 57 pulse-beats, when lying down. Tmx=100. Frequent extrasystoles.

Record no. 7.

Radial tracing rhythmic and regular, with extrasystolic interruptions. Slow pulse, 53 beats per minute. The jugular tracing shows that the extrasystoles are of ventricular origin. There are two extrasystoles to be seen in this tracing; the first rather anticipated the *c* rise coinciding with the *a* wave: the second still more anticipated the *c* rise coinciding with the ascending phase of the *a* wave. Auricular rhythm unchanged. The *a c* interval lengthened after the extrasystoles.

Summary: ventricular extrasystole, slow heart. At the extreme right of the tracing an interpolated extrasystole.

Observation no. 9.

Ventricular extrasystoles. Cardiac insufficiency.

M. R., negress, 30 years, resident at Santa Rita.

Signs of marked cardiac insufficiency; rate 82 per minute, with frequent extrasystoles. Tmx=110. Large goiter. Thyroid much increased in size.

This woman is the mother of the patient Geraldo, who was in the hospital with diplegia.

Record no. 8

The only remarkable thing about this tracing is the extrasystoles of ventricular origin.

Observation no. 10.

Ventricular extrasystole. No signs of cardiac insufficiency. Atropine test.

B. C., white, male, 44 years, married, farm laborer, resident at Trahyras.

Examined March 23, 1913.

Previous history as in the preceding case; only intermittent fever. This patient came to cousult us on account of a strong facial neuralgia which had lasted for 5 days. He is moderately tall and well built. No subjective symptoms. Heart not enlarged. Heart sounds without noticeable alterations, with the exception of tympanism of the second sound in the aortic area. Pulse with numerous extrasystoles. Pulse 64 when lying down, standing 75. The atropine test accelerates the pulse and makes it more regular. Liver and spleen not noticeably enlarged. Thyroid enlarged, with a cystic nodule.

Records 9 and 9-A.

I) The radial tracing shows frequent extrasystolic beats, which interrupt the rhythm. The extrasystoles are ventricular, as may be seen in the venous tracing.

II) An hour after injection of 0,g001 of atropine the pulse is perfectly regular and slightly accelerated.

Observation no. 11.

Ventricular extrasystole. Dilatation of the heart. Atropine not modifying the extrasystoles.

C., white, male, 13 years, resident at Muquem.

Examined October 24, 1913.

Previous history. Malaria with recent attacks of fever. This patient complains of gastric pains, a feeling of gastric fulness and sometimes has attacks of giddiness. He does not complain of dyspnea, palpitation or any other symptom. Heart enlarged, apex beneath the fifth rib in the mammillary line, 8,5 cm. from the midsternal line. First sound muffled. Second reduplicated. Mesosystolic murmurs in pulmonary area. Pulse 84 per minute, with frequent extrasystoles. Tmx.= 110. The atropine test accelerates the heart beats (105 per minute). Liver not enlarged. Spleen enlarged and painful on pressure. Thyroid increased in volume. Inguinal glands enlarged.

November 24, 1913. Pulse rate 85. No change in the physical signs of the heart. Numerous extrasystoles.

January 15, 1913. No modifications in the physical signs of the heart. Numerous extrasystoles. Number of beats 90 when lying down and 104 standing; the extrasystoles are as numerous in one position as in the other.

Record no. 10.

The rhythm of the pulse is interrupted by extrasystolic beats of ventricular origin. There is also a slight sinus arrhythmia.

Observation no. 12.

Ventricular extrasystole; the atropine test makes the rhythm regular.

V. D., mulatto, 35 years, widow, resident at Lassance.

Examined April 18, 1913.

Previous history, only attacks of intermittent fever.

Complains of occasional attacks of palpitation. No other subjective symptoms.

Heart increased in volume, apex beat in the fourth intercostal space, in the mammillary line, 8, 5 cm. from the midsternal line.

No noticeable change in the heart sounds. Pulse 76, with frequent extrasystoles.

Katzenstein	before—76 ps.	? Tmx.	130.
	during—82	»	120.
	after—80	«	125.

Pulse 92 standing. Liver not enlarged. Spleen enlarged, with a thin, hard margin. Glands not hypertrophied. Thyroid with moderate goiter. Her husband died suddenly.

Records no. 11 and 11-A.

1) Radial pulse full, rather slow, rhythmic, the dominant rhythm interrupted by extrasystoles with ample compensating period. Rate little less than average, 68 per minute. Extrasytoles frequent. and scattered irregularly in the tracing. The venous pulse with strongly accentuated carotid waves; *a* waves well marked. *v* waves slightly marked.

Corresponding to the extrasystoles of the radial pulse there are exaggerated rises of the jugular pulse due to the simultaneous contraction of auricle and ventricle. The auricles contract rhythmically; the contraction of the ventricles is anticipated. Ventricular extrasystoles.

II) Taken after injection of 0g,001 of sulphate of atropine. Rate increased; from 68 to 92. Disappearance of the extrasystole. Radial pulse rhythmic and regular. Venous pulse with carotid appearance. Ventricular extrasystoles in the heart, rather slow; disappearance of the same half an hour after atropine, with moderate acceleration, 68; 92.

Observation no. 13.

Ventricular and nodal exstrasystoles. Palpitation.

A. C., mulatto, 40 years old, male, single, laborer, resident at Beltrão.

Examined March 3, 1913. In his history there is only a reference to intermittent fever that he had some months previously, from which there remains pain in the right hypochrondrium. At present, aside from this pain, he complains of attacks of palpitation which are transient and infrequent. No other subjective symptoms elicited. Heart not enlarged. Heart-beats interrupted in their rhythm by extrasystoles in bigeminal series. Sounds normal. Pulse 78, one beat being strong and one extrasystolic. Tmx. 110. After the injection of 0,001 g. atropine the pulse becomes regular, 92 lying down and 115 standing. Liver and spleen are a little enlarged. Thyroid enlarged with a voluminous goiter.

Records no. 12, 12-A and 12-B.

(I This tracing shows a type of bigeminal pulse caused by ventricular extrasystoles which succeed each other in alternating cycles. The legend explains itself.

II) Tracing taken fifteen minutes after injection of 0g,001 of atropine. The succession of bigeminal beats is interrupted by a trigeminal group. This group seems to be formed by the addition of an auriculo-ventricular extrasystole to the ventricular extrasystole. The *a* wave which is fused with the *c* wave of the first extrasystole belongs to the dominant rhythm; the second *a c* is due to the fusion of two synchronous extrasystolic waves. The auricular rhythm regains its rate from the extrasystolic auricular wave.

III) Taken one hour and twenty minutes after atropine. The pulse has become regular and the rate somewhat increased.

Observation no. 14.

Ventricular extrasystoles. Cardiac insufficiency. Palpitation.

J. L., mulatto, 34 years, male, married, farm laborer, resident at Bagre.

Examined April 14, 1913.

The patient had convulsive attacks up to the age of 18 when they ceased. He also had intermittent fever about twelve years ago. There is nothing worth mentioning in the previous history of this man who was strong and hardworking until the beginning of his present illness, about a year ago. After an attack of "Dysentery" has suffered

from pains in the legs and vague pains in the body. These were followed by palpitation. precordial pulsation which extended to the veins of the neck and were felt in the ears: the beats are strong and provoked by emotion or exertion, or come on even while the patient is quiet or during sleep, so that he wakes with a start. He is fatigued by the slightest exertion and scarcely able to walk 20 or 30 meters without fatigue accompanied by palpitations and cold sweat. Abundant sweating even when quiet. Gastric disturbances; the ingestion of food causes much agony ("avexame").

Cardiac percussion area not increased. Apex beat at the fifth intercostal space, 7.5 cm. outside the midsternal line; right margin 2,5 cm. from the midsternal line. Heart sounds without noticeable change. No murmurs; 76 beats with numerous extrasystoles in bigeminal series.

Katzenstein	before — 76 ps.	Tmx.	130
	during — 82 «	«	130
	after — 72 «	«	130

Atropine test. Pulse 108 standing.

Liver not enlarged nor painful on pressure. Spleen not enlarged. Thyroid not noticeably enlarged. Inguinal glands slightly enlarged. Further examination on July 13, 1913. For some time the patient showed marked improvement, but a fortnight ago he became worse again. The old disturbances appeared anew with increased edema of the face. Cardiac area not modified. First sound reduplicated; the second accentuated in the pulmonary focus. 70 pulsations with extrasystoles. Tmx.=135. Liver slightly enlarged and painful.

July 24, 1913.

Pulse in vertical position, 100. Occasional extrasystoles.

Katznstein	before — 72 ps.	Tmx.	145.
	during — 72 «	«	140.
	after — 78 «	«	140.

Record no. 13.

The radial pulse is irregular on account of the interpolation of numerous ventricular extrasystoles, which are easily seen by the legend.

13 *a*) After the injection of atropine the number of extrasystoles diminished considerably, only one being recorded in a number of tracings. It was of ventricular origin.

Observation no. 15.

Ventricular extrasystoles. Fainting attacks.

S. A., 36 years, female, resident at Santa Rita.

Examined April 2, 1911.

Marked melanodermia. Absence of arteriosclerosis. Large goiter. Cervical glands enlarged. In the last few days the patient has had fainting fits. Liver not enlarged.

Katzenstein	before — 91 ps.	Tmx.	105
	during — 78 «	«	105
	after — 91 «	«	105

Numerous extrasystoles.

Record no. 14.

The radial and cardiac tracings show strong arrhythmia, but the dominant rhythm is to be seen in the group of pulsations to the right of the central vertical line. This rhythm is interrupted by numerous extrasystolic beats. The combined analysis of the 3 tracings elucidates the nature of these extrasystoles. In group I, II, III, IV. The beat *IV* is of ventricular extrasystole as the legend shows. The group a, b, c, d, f, is more complex. To 5 auricular beats there are 6 ventricular ones. This is because the extrasystolic beats *c* and *d* succeed each other rapidly. The *a* III wave falls within the refractory period of the cycle and is blocked. The premature beat *c* is anterior to *a* IV being very much anticipated and does not prevent the excitation of the latter being transmitted to the ventricle, increasing only the time of conduction. The beat of cycle (d) might he considered dependent on *a* III, with very much delayed rate of conduction of the stimulus. The polygraphic tracing is not sufficient to elucidate the case. The

beats marked on the left of the tracing are susceptible of the same interpretation.

Observation no. 16.

Ventricular extrasystole. Cardiac insufficiency. Spasm of the esophagus.

J. G., white, male, 39 years old, resident in Beltrão.

April 7, 1911.

The patient complains of palpitation, fatigue on exertion and nocturnal attacks of suffocation and giddiness. He also has difficulty in swallowing solid food, spasms of the esophagus, which oblige him to drink water after every mouthful. Well-marked bronze coloring. Large goiter. Spleen slightly enlarged. 110 beats when lying down, 130 standing. Tmx. 115. Numerous extrasystoles.

Record no. 15.

April 7, 1911.

Radial pulse with regular dominant rhythm, with slightly increased rate, 83 per minute; interrupted by extrasystolic beats which occur irregularly. The extrasystolic beats have a complete compensating period of rest. Jugular pulse; the *a c v* waves occur in the normal succession; wave *c* in some points hardly noticeable. Wave *a* not raised. In the cycles interrupted by extrasvstoles, the latter only appear synchronously with the auricular contraction, whence the fusion of waves *a* and *c* indicated by the legend. Auricular rhythm not modified except slightly by the respiratory movements. The extrasystoles are of ventricular origin and more or less premature.

Summary: ventricular extrasystoles occurring irregularly.

Observation no. 17.

Ventricular extrasystole. Bigeminism.

M.M.; 38 years old, female, resident at Porto-Faria.

April 19, 1911.

Complains of lumbar pains and pains in the stomach. Frequent attacks of palpitation. Large goiter. Melanic pigmentation well-marked. Liver increased in size; 90 heart beats with extrasystoles in bigeminal series. Tmx.=125.

Record no. 16.

This is a tracing of bigeminism of heart and pulse with an intercalated trigeminal group. The bigeminism is produced by the regular succession of ventricular extrasystoles with compensating period of rest. The trigeminal group is formed by the intercalation of an interpolated extrasystole in the cycle. The *a c* interval which corresponds to the beat of normal cycle which succeds the extrasystole is very much increased and the next *a* wave is blocked.

Observation no. 18.

Ventricular extrasystole. Bigeminism. Spasm of the esophagus (Mal de engasgo—Difficulty in swallowing.)

Examined May 23, 1913.

Previous history; all that is worthy of notice are pains in the joints which appeared when the patient was 18 years old, and which recur on cold and damp days. For about three years the patient has had palpitation. Feeling of limpness in the body and pains in the legs. Dyspnea on exertion and inability to work as well as his fellow-laborers, being easily tired. Nocturnal dyspnea. Giddiness. Sensation of distension of the stomach with acid eructations. Choking. Sometimes the patient cannot swallow his food without the help of water. Heart slightly enlarged. Apex beat in the fifth intercostal space a little inside of the nipple, 9,5 cm. from the midsternal line. Apex shock large and strong. No noticeable change in the heart sounds. Pulse 65 per minute, ample, full, and unstable, the number of beats changing from one moment to another. Acceleration of the pulse after swallowing. Frequent extrasystoles, at times isolated, at others in bigeminal series.

Record no. 17.

The waves of the radial and of the venous pulses are found in this tracing. The radial pulse shows a very clear bigeminism. At the right side of the tracing there are regular waves of the dominant rhythm to be seen. The bigeminism arises from the succession of ventricular extrasystoles in alternating cycles. The venous tracing confirms this interpretation, the auricular waves fall rhythmically; at one time the ventricular wave preceding the normal beat at, another succeeding that of the premature one, falling in the final phase of the systole of the latter.

Observation no. 19.

Bigeminism from nodal extrasystoles. Interpolated extrasystole. Atropine test with change of conductibility.

J. Q. R.; white, 25 years, old, male, tradesman, resident at Sant'Anna dos Alegres. Previous history, merely different attacks of colds and bronchitis *a frigore*. Denies having had venereal or malarial history. About five years ago a beginning of *ankylostomiasis* with pains in the legs and fatigue, which was cured. He has felt ill for about a year, and has had attacks of precordial strong and rapid beats. At first short and far between, these attacks have become more intense, more frequent and of longer duration. They are brought on by the slightest emotion or effort or even come on without any provocation. They are independent of meals. Sometimes they come on at night and the patient wakes up with a start. They are very uncomfortable and bring on uneasiness, spots before the eyes, sweating, trembling, labored breathing and strong agony (avexame). The patient does not mention giddiness. For about two months he has had a feeling of fatigue after any effort, even after the slight exercise of walking, which brings on tiredness, palpitation and pains in the legs. He does not mention edema, nor has he any. Heart enlarged, apex beat in the fifth intercostal space outside the mammillary line. Right margin 2,5 cm. from the midsternal line. Sounds without noticeable change. No murmurs. Extrasystoles with bigeminal appearance. 72 to 80 pulsations- Tmx.=135. Atropine test. Liver not enlarged. Thyroid enlarged. Inguinal glands not enlarged. Nervous system negative.

Record no. 18.

Tracing *I* was taken before the injection of atropine. The tracing of heart and pulse which are analogous show waves in bigeminal groups interpolated with regular waves of the dominant rhythm between. The second wave of the bigeminal group is of extrasystolic appearance; the jugular tracing shows that they are "nodal extrasystoles"; the auricular and ventricular contractions are premature and synchronous. The dominant rhythm is slow; the jugular curve tracing is peculiar as it shows a bifid *V* wave and very clear Hirschfeld *C* waves. The *a* wave of the dominant rhythm which follows the extrasystole is slightly anticipated.

Summary: bigeminism caused by nodal extrasystole.

Record no. 18-A

Taken fifteen minutes after the injection of atropine.

The pulse has become regular, but not entirely so. The *a* waves do not succeed each other in perfectly regular rhythm; an extrasystole corresponding to *c' v'* of the venous curve is to be seen.

Record no. 18-B

Taken one hour after atropine. The beats are slightly accelerated and are becoming rhythmic.

Record no. 18-C

Taken four hours after atropine. The pulse has again become irregular though it still is accelerated. The *a* waves succeed each other irregularly. Some are blocked,

which explains the lapses of the radial pulse. The change in conductibility which appears many hours after the action of the atropine is interesting; this is not seen in other tracings. Here also the variations of the dominant rhythm are much greater.
Some beats *(a' c')* are probably auricular extrasystoles.

Observation no. 20

Interpolated extraventricular systoles. Palpitations. Cardiac insufficiency.

Examined December 29, 1912.

M. F., mulatto, 40 years, female, married, resident at Santa Rita. For some months the patient has suffered from "agony" with great fatigue, anxiety and uncomfortable heart beats. Dyspnea when lying down. Palpitation; attacks of strong and rapid beats, sometimes provoked by exercise, by standing or even coming on when the patient is quiet without any special reason. Sometimes the beats are slow and strong. Gastric uneasiness after swallowing, the ingestion of food provokes agony. She feels better when she is fasting. Frequent and abundant eructations. A feeling of depression and general weakness. Lack of appetite. Heart but slightly enlarged, measuring 10,5 cm. at the base; apex beat 8 cm. from the midsternal line, a slight downward dislocation of the heart; Sounds clear, the second somewhat tympanitic at the aortic area. Beats rhythmic, the rhythm interrupted by extrasystoles, either in series or singly. Pulse 60 per minute. Tmx. 140. Pulse small and hard. Liver much enlarged. Spleen without noticeable enlargement. Thyroid gland with cystic goiter.

Further examination January 1, 1913.

Frequent attacks of giddiness. Buzzing in the head, vague pains in the body. Frequent palpitation, sometimes attacks of strong rapid beats, at others strong and slow beats. At the time of examination, the patient complained of agony and had strong slow beats but the objective examination revealed nothing abnormal. Pulse 50 beats per minute: no dyspnea. Sometimes the beats were so rapid that the heart seemed to tremble. Condition of the heart same as before. Generalised edema. Liver still much enlarged.

January 19, 1913.

No more edema. Liver a little smaller. Improvement of the subjective symptoms. Physical state of the heart unaltered.

June 4, 1913.

After a period of improvement the patient, being worse, came to consult us again. There was nothing, however, which called for special interest. After a few days treatment she got better.

Record no- 19.

This tracing is interesting because it shows trigeminal rhythm caused by the interpolation of ventricular extrasystoles every four cycles, with a quartan rhythm.

The indication of the waves shows that the extrasystoles are interpolated,

Observation no. 21.

Interpolated ventricular extrasystoles.

M. I. do N., white, female, 27 years old, married, field-laborer.

Examined October, 1914.

The patient has been married for thirtem years and has had three miscarriages at three months and five children born at term; she lost a child of three from sore throat. The last child is 18 months. First menstruation at the age of 12, regular and painless. Has had intermittent fever. Heart beats, fatigue and agony, she feels worse at rest and improves with exercise. The heart-beats accompanied by giddiness and tremblings. Vague headaches. Trembling.

Heart. Apex beat in the fourth intercostal space, 7,5 cm. from the midsternal line. Tmx=150. 74 pulsations per minute. Extrasystoles frequent after exercise and exertion. Liver extending 19 cm. from mammillary line. Spleen not palpable. Goiter with cysts of different sizes.

Record no. 20.

An interesting formation of trigeminal rhythm by the regular intercalation of ventricular extrasystoles. They appear every 3 cycles, in tertian rhythm. Compare with record 19.

Observation no. 22.

Ventricular extrasystoles in series.

P. F. S., white, male, 45 years, resident at Coração de Jesus. Signs of cardiac insufficiency, Katzenstein's test positive. Heart sounds muffled. Frequent extrasystoles. Liver enlarged and painful on pressure. Thyroid much enlarged. Cervical glands eniarged.

Record no. 21.

The dominant rhythm is interrupted by a series of six consecutive extrasystolic beats. These beats are due to extrasystoles of ventricular origin; in another part of the tracing is seen an isolated extrasystole which is also ventricular.

Observation no. 23.

Ventricular extrasystole. Post-extrasystolic alternation. Palpitation. Marked dilatation of the heart.

C. C. da S. mulatto, male, 27 years, married, farm laborer, resident at Porto Faria.

Examined September 12, 1912.

No subjective signs, except occasional passing attacks of palpitation. The patient is tall, above middle height, well-built and of robust appearance. Heart not enlarged, apex beat in the fifth intercostal space outside and below the nipple, 14 cm. from the midsternal line. Right margin 6 cm. from the midsternal line. Heart sounds without any marked alteration. No murmurs. Pulse lying down 82, standing 107.

Katzenstein { before – 81 / during – 92 / after – 92

Tmx=125.

Pulse with numerous extrasystoles Liver slightly enlarged. Spleen not noticeably enlarged. Goiter, thyroid gland moderately enlarged.

Record no. 22.

Besides the falling out of the radial pulse corresponding to the slight beats of the cardiac tracing, there is a very marked alternation in the beats which follow the lapses, which are extrasystoles and are not registered in the pulse. These are ventricular.

Record no. 22.

The sphygmogram registers the interruption of the rhythm by extrasystolic beats and lapses. The alternation of the pulse in also noticeable and more apparent in the pulsations that follow an extrasystole. The extrasystoles are ventricular.

Observation no. 24.

Ventricular extrasystoles. Alternation of the pulse.

T. X., male, 31 years, resident at Belém.

The patient came to consult us on account of fatigue, palpitation and gastric disturbances.

Heart enlarged, apex beat in the sixth intercostal space outside the mammillary line, the base measuring 16,3 cm. Pulse arrhythmic, with lapses which correspond to the extrasystolic beats in bigeminal series. Pulse 76 lying down, 74 standing up. Tmx=110. Thyroid enlarged with cystic goiter of the middle lobe; cervical and axillary glands enlarged. The patient came back to consult us three months later and was put in hospital as he showed intense signs of cardiac insufficiency, which brought on asystole.

He was observed by a commission of professors who were there at the time. This case was considered very interesting from a clinical point of view and one of the best examples of the cardiac form. Furthermore

an autopsy of this case was performed and showed for the first time the presence of parasites in the chronic form of the disease.

Record no. 23.

In the radial tracing were seen extrasystoles with complete compensating repose, possibly ventricular, and marked alternation.

Observation no. 25.

Extrasystole. Palpitation. Post-extrasystolic alternation.

C. L. A., mulatto, female, 30 years, resident at Contendas.

Examined January 1, 1913.

Has been ill for a year until which time she was strong; there is no history of previous disease. For about a year she has had frequent headaches, lack of appetite, difficult digestion, gastric pains, to which were added later on limpness, pain in the legs, weariness and heart palpitation, provoked by the slightest effort At present it is the palpitation that disturbs most, as it comes on the least exertion or even while at rest. Neither nocturnal dyspnea. nor edema. Heart not enlarged. First sound unchanged, second with a pulmonary accentuation. Mesosystolic murmur at the pulmonary area. Cardiac erectism, with very visible pulsation of the veins of the neck. Pulse unstable, the number of beats varying from 98 to 112. Tmx.=125. Very numerous extrasystoles at the beginning of the examination afterwards diminishing. Liver and spleen not enlarged. Thyroid enlarged.

Record no. 24.

Radial pulse with dominant rhythm interrupted by ventricular extrasystolic beats; in the venous tracing the *a* wave of the auricular rhythm and the *c'* wave of the premature ventricular beat are fused. The interval *a c* unchanged. In the radial tracing a post-extrasystolic alternation is indicated.

Observation no. 26.

Ventricular extrasystole, Post-extrasystolic alternation. No subjective symptoms.

F. R. A., white, male, 26 years, widower, farm laborer, resident at Bebedouro.

Examined December 7, 1912.

Previous history: about 10 years ago was jaundiced, edematous, with easily brought on fatigue and palpitation; he was cured. The patient has also had several attacks of ill defined fever.

At the present date he is strong, inclined to work, without dyspnea on exertion. No edema. He came to consult us on account of a traumatism of the thorax which left a local pain, about 20 days ago. No enlargement of the cardiac area, apex 7, 5 cm. from midsternal line, below and within the nipple; the right margin 3,5 cm. outside the midsternal line. Tachycardia: Pulse 102, with numerous extrasystoles. During the examination he complained of uncomfortable heart-beats (emotion). Liver not enlarged. Thyroid much enlarged.

Record no. 25.

The radial tracing shows very marked alternation of the pulse principally after the extrasystoles, which are ventricular as shown by the venous pulse. The cardiac tracing shows, besides the respiratory oscillations, very marked auricular waves besides the ventricular waves.

The jugular tracing is not disturbed; the *a* waves succeed each other in even rhythm. The high points which are seen on the tracing arise from the fusion of *a* and *c'*. Ventricular extrasystoles coinciding with the auricular systole.

Summary: Ventricular extrasystole with marked alternation.

Observation no. 27.

Ventricular extrasystole. Post-extrasystolic alternation.

F. X., white, male, 55 years old, resident at Beltrão.

Examined May 4, 1911.

The patient complains of vague pains in the extremities and palpitation. Very marked bronze coloring. General emaciation. Pulsation; 76, with occasional extrasystoles. Tmx.=100. Pulse standing, 108.

Record no. 26.

The appearance of the radial tracing is that of a series of rhythmic beats, interrupted by lapses and slight extrasystolic beats. The lapses and the extrasystolic accidents take in the space of 2 or 3 normal beats, according as to whether there are 1 or 2 extrasystolic beats; full compensating period of rest. The post-extrasystolic alternation is well marked and lasts during many beats after the extrasystole. It is well marked on the whole of the right side of the tracing; 20 beats after the extrasystolic one.

Observation no. 28.

Ventricular extrasystoles.

M. L., de M. mulatto, male, 28 years resident at Santa Maria.

Examined April 29, 1911.

He complains of giddiness, palpitation and precordial pains. Pulse arrhythmic, with frequent extrasystoles, sometimes in bigeminal series. Pulse 62: Tmx.=110. The extrasystoles are of ventricular origin; the a—c intervals lengthened, as may be seen in the tracing. Thyroid very much enlarged, with goiter.

Record no. 27.

The radial pulse is interrupted in its rhythm by premature beats of ventricular origin, shown in the venous tracing by high waves; fusion of *a'* and *c'*. A slight lengthening of *a c* interval is also noticed; this is a sign of a slight alteration of conductibility.

Observation no. 29.

Extrasystoles. Lengthening of a—c. Sudden death.

L. J. V., mulatto, male, 35 years, laborer, single, resident at Urucuia.

Previous history: patient only mentions having had intermittent fever several times. Denies venereal disease. Robust constitution, apparently strong. Skin pale, slight generalised edema, more marked in the face. Has been feeling ill for about eight years. His legs are weak and he has cramp at night. Palpitation, coming on sometimes when at rest, at other times on exertion; precordial pulsation, also in the veins of the neck; these beats are strong and uncomfortable; dyspnea on exertion and nocturnal dyspnea. Frequent cough. Constant sensation of gastric fulness, with great discomfort and respiratory difficulties, increased by taking food, however small the quantity. These symptoms have gradually increased so that patient can no longer work. Heart considerably enlarged. Apex beat in the sixth space, 15 cm. from the midsternal line, reaching to the axillary line; right margin 5 cm. from the midsternal line. Precordial shock diffuse, apex shock ample and intense. Heart sounds muffled, especially at the base. No murmur. Bigeminal beats; the second beat has at times two tones, at others only one, simulating the auricular systolic beats which are not transmitted, being very muffled. Pulse slow; sometimes the extrasystolic beats of the bigeminal group are felt in the pulse, at other times this is not the case. Pulse 46; Tmx.=135. The number of beats varies but slightly with the difference of position or on exertion. Lying down 55, standing 58, after exercise 56. Atropine test: bigeminism not modified-beats accelerated: 80 per minute (v. tracing), Left lobe of liver slightly enlarged and painful on pressure. Spleen enlarged, not painful. Thyroid enlarged with cystic nodules.

August 17, 1913. Edema disappeared and all the symptoms improved without any change in the physical condition of the organs. August 20, 1913. Gastric uneasiness more intense. Strong palpitation. Increase of dyspnea on exertion. 58 beats when standing, lying down 56. Bigeminism. Tmx.=120. Physical condition of organs unchanged. On going out from the hospital for a short walk this patient died suddenly.

The histopathologic examination of the heart was made by Professor B. C. Crowell, who found lesions peculiar to trypanosomiasis, this case being one of those which enabled him to establish the histopathologic characteristics of the cardiac lesions in the chronic form of Chagas' disease.

Record no. 28 and 28-A

I) The radial tracing is that of a slow arrythymic pulse, with cycles varying very much in length; in some there are extrasystolic beats.

The cardiac tracing is of bigeminism; the groups of bigeminal beats vary in their succession. Some of the auricular waves are well marked in some points of the cardiogram.

The first beat of the extrasystolic group is of the dominant rhythm. The jugular pulse shows that it is always preceded by an auricular wave and that the *a—c* interval is lengthened. The second beat of the bigeminal group is extrasystolic. The origin of the extrasystoles is in some points frankly auricular. Others seem to be auricular, like that which accompanies the radial beat II and that which is marked in the right half of the tracing. Others are probably nodal, like those which are registered by acute and high waves in tracing II.

II) The rate of the auricular waves is arrhythmic and some are blocked. The causes of the arrhythmia of the pulse are consequently multiple and very difficult to analyse. Atropine had no appreciable action to be seen on the tracing, except acceleration.

Observation no. 30.

Extrasystole. Lengthening of the a—c interval.

D. M. da C.; negress, 60 years old, widow, resident in the neighborhood of Lassance.

Examined March 9, 1913.

Previous history obscure, intellect of very low order, so that it is very difficult to question the patient. She complains of palpitation, dyspnea on exertion, dyspnea when lying down and at night, so that she cannot sleep. No edema. Heart much enlarged, apex beat outside the mammillary line at 11 cm. from the midsternal line. Right margin 4 cm. outside the midsternal line. Irregular beats with numerous extrasystoles sometimes in bigeminal series. Sounds muffled, no murmurs. Pulse 56, irregular and arrhythmic.. Tmx.=145 Left lobe of liver slightly enlarged. Spleen not palpable. Nervous system negative. Thyroid enlarged.

Reexamined April 19, 1913. Dyspnea on exertion, when lying down and at night. Sleeplessness. Generalised though slight edema. Bases of the lung congested. Frequent cough. Heart enlarged; apex beat in the fifth space on a level with the anterior axillary line. Heart sounds muffled, principally the first. Marked swelling of the neck veins, with scarcely noticeable pulsations. Pulse 55. Liver rather enlarged.

Record no. 29.

The radial and cardiac tracing show bigeminism, with some beats of the dominant rhythm at the right side of tracing. The second beat of the bigeminal group is extrasystolic; the extrasystoles are nearly all ventricular. The marking of the tracing indicates our interpretation of it; *a c* interval lengthened so that the conduction of the contractile stimuli is delayed.

Observation no. 31.

Ventricular extrasystoles. Lengthening of the a—c interval.

M. P. dos S.; mulatto, female, 33 years, married, resident at Lassance.

Examined April 18, 1913.

Has been ill for about twelve years and thinks her illness began after child birth, when she had fever for fifteen days. Her subsequent confinements aggravated her condition and after the last, a year ago, she became much worse. Present condition: Slight icterus. Cyanosis. Edema of the lower, extremities and trunk, however not very

marked. Headache and vague pains in the body. Cardiac palpitation, dyspnea on exertion and even attacks of dyspnea when at rest and at night so that she cannot sleep. Refractory cough, the last few days bloody sputum. She has had edema of the legs. Patient feels that the stomach is swollen. For the last few days has had attacks of vomiting accompanied by great anxiety. Nearly incessant cough and dyspnea. Lack of appetite. Constipation. Heart much enlarged, apex beat in the sixth space, slightly within the axillary line, 15 cm. from the midsternal line. Right margin 5 cm. from the midsternal line. Precordial region with a rounded prominence. Strong precordial shock, shaking the thoracic wall, its violence being especially noticeable in the fourth, fifth and sixth spaces. First heart sound muffled with slight murmur at the apex, without propagation. Second sound accentuated in the pulmonary area. Pulse weak, soft and empty. Extrasystolic arrhythmia. Number of pulsations varying from 88 to 92. Tmx=110. Liver much increased in size, painful on pressure. Spleen without noticeable enlargement. Thyroid enlarged. Congestion of the bases of both lungs, the right more marked.

The patient was reexamined on June 20, 27 and 28, and on July 3 and 5. She was only slightly better and did not come back for consultation after the fifth. On that day her condition was as follows: Dyspnea as well as general condition improved. Pulse 82, sometimes in bigeminal series. No more vomiting.

Record no. 30

The radial pulse is entirely arrhythmic but not that of complete arrhythmia. Analysis of the venous and pulse tracings shows that the arrhythmia is produced by different causes. The first is a change in the auricular rate, the *a* waves appearing irregularly spaced. The conductibility is changed, the *a c* interval lengthened; this induces a delay in the conduction of the contractile stimulus. Extrasystolic beats of ventricular origin. The legend of the tracings shows these alternations, as well as their interpretation clearly.

Observation no. 32.

Ventricular extrasystole. Lengthening of the a—c interval. Marked cardiac insufficiency.

O. N. C.; mulatto, male, 38 years, farm laborer, resident at S. João da Ponte.

Examined September 12, 1912.

He has been ill for about two months; fatigue on exertion gradually increased. Pale, slight edema of face and lower extremities. Dyspnea on exertion and at night. Cardiac area much enlarged. Apex beat in the fifth intercostal space, 12 cm. from the midsternal line. Right margin 4,5 cm. from the midsternal line. Systolic murmur at apex, replacing the first heart sound with propagation towards the axillary line. The firts sound can be heard in the tricuspid area. Second sound reduplicated with pulmonary accentuation. Pulse 88; seated 99. Numerous extrasystoles. Tmx.=105. Liver enlarged painful on pressure. Spleen with noticeable enlargement. Thyroid enlarged, with voluminous goiter.

Record no. 31.

The radial pulse shows very clear alternation, extrasystolic lapses and beat with compensating complete repose. The jugular pulse shows the premature beats *c'* of ventricular origin, coinciding with the auricular beats *a* of the dominant rhythm.

It can be seen that the conductibility is altered, there being delaying of the conduction which is indicated by the lengthening of the *a—c* interval.

Observation no. 33.

Ventricular and nodal extrasystole. Tachycardial crises. Lengthening of the a—c interval. Ventricular escape.

P. A. S.; mulatto, male, 39 years, married, resident at Contria.

Examined February 17, 1913.

Previous history of only blenorrhagia and intermittent fevers. Until about two and a half years ago the patient was strong and hard working. About that time he began to feel fatigue on exertion, dislike for work gastric fulness almost always present, increased by the ingestion of food. Dyspnea on exertion aud when lying down. Attacks of dyspnea even when at rest. Nocturnal dyspnea which interrupts the sleep. Frequent palpitation; attacks of strong, rapid, inconvenient, uncomfortable, and at times painful, heart beats coming on without noticeable cause even during sleep, causing him to wake with a start. These attacks are quickly over, not lasting more than half an hour. Frequent giddiness, but not enough to make him fall. As to the feeling of gastric fulness, the patient states that sometimes he feels "as if he had a ball in his stomach which came up to his throat and choked him". The patient is below average height, of cretinised appearance, his skin of a dirty yellow color; large goiter. Generalised edema. Heart much dilated. Apex beat in the sixth space, a little within the anterior axillary line. Right margin 4,5 cm. from the midsternal line. Precordial area with a rounded prominence. First sound silent at the apex, replaced in the tricuspid area by a systolic murmur. Second sound reduplicated with pulmonary accentuation. Arrhythmic pulse. with frequent extrasystoles. Pulse 88 to 90. Tmx.=120.

Arteries slightly hardened. Liver enlarged and painful on pressure. Spleen slightly enlarged. Examination of lungs negative. Examination of nervous system negative.

Feb. 21. All the subjective phenomena are better. Diminished edema. Physical signs not changed. 76 radial pulsations with numerous extrasystoles.

Feb 25. The patient is better and the edema has largely disappeared. Size of heart very little changed. No more tricuspid murmur. Pulse arrhythmic, with attacks of tachycardia. Liver not noticeably enlarged. He came to consult us again on March 9, 1913. Palpitation diminished. There had been no more dyspnea. There is no change in the area of cardiac dulness. Pulse 72 with numerous extrasystoles. Tmx.=115. Liver not noticeably changed. Heart sounds muffled, with very clearly heard tricuspid murmur.

March 11, 1913. General condition better. No more tricuspid murmurs. Arrhythmic beats in bigeminal series, alternating with series of rapid beats. Liver slightly diminished.

March 14, 1913.

Slight aggravation of the subjective symptoms. The tricuspid murmur had reappeared.

March 15, 1913.

Improved again, Diminished palpitation. The improvement is more evident, and the patient left three days later.

We heard that he died some months afterwards in asystole.

Records nos. 32, 32-A, 32-B, 32-C.

I) The radial tracing is very arrhythmic, also the cardiac one.

The arrhythmia is of very complex origin and only the joint examination of the three curves can explain it.

At the left in the center, and at the right side of the radial tracing are seen groups of beats of the dominant rhythm, with a rate of 83 beats per minute, but the cycles are not perfectly equal. The examination of the waves of these cycles on the venous tracing shows the *a c* interval to be much lengthened, which indicates an alteration in conductibility. In the cardiogram the auricular wave is clearly marked in the diastolic phase of the ventricles. The first extrasystolic beat which appears after the fifth beat of the normal cycle is an extrasystole, intervening between the fifth and sixth beats of the dominant rhythm. The *a c* interval of the sixth beat is lengthened; the ventricular systole is so retarded that it falls in a refractory phase and is blocked, leaving a long pause between the sixth and seventh beats. The interval between the fifth and seventh beats in the dominant rhythm is perceptibly equal to three times

the normal cycle. The followyng extrasistole is ventricular. The beat which follows the extrasystole begins a series of beats of the dominant rhythm; its cycle is lengthened by the retardation of the following ventricular systole, on account of the delay in the conduction of the contractile stimulus. The *a c* interval is lengthened.

Thus the arrhythmia comes from ventricular extrasystoles, interpolated or otherwise, and from the alteration of the conductibility.

II) The tracing shows a tachycardial crisis with a rate of 130 beats per minute. The radial pulse shows a very noticeable alternation. Jugular pulse with high rhythmic waves at the same rate as those of the radial pulse, which are the auricular waves coinciding with the ventricular waves of the anterior cycle that are marked at the origin of the *a* waves. The tachycardial crisis is therefore probably due to a succession of auricular extrasystolic waves at a rapid rate transmitting themselves to the ventricle with delay. The *a c* interval much lengthened. At the right side of the tracing are seen some beats of the dominant rhythm and many extrasystolic beats.

III) This shows bi and trigeminal rhythm from ventricular extra-systoles.

IV) Tracing 32-*c* shows the effect of digitol.

The effect on the conductibility is manifest; the *a c* interval is much lengthened, having apparently at some points "ventricular escape". Numerous extrasystoles in bi- and trigeminal groups.

Observation no. 34.

Ventricular extrasystole. Lengthening of the a—c interval. Cardiac insufficiency.

J. D., mulatto, male, laborer, married, resident at Contria. Previous history only mentions intermittent fevers. For a long time he has been subject to attacks of palpitation, without having his general condition affected. About a year ago the patient began to feel weakness in the legs and dyspnea on exertion which increased gradually, preventing him from working. Lately he has had dyspnea from lying down, also at night, a cough, and edema of the lower extremites and face. The palpitation has considerably increased in frequency and intensity; it may be even brought about by drinking water. Heart much enlarged. Apex beat in the sixth space, near the anterior axillary line, 13 cm. from the midsternal line. Right margin 4, 5 cm. from the midsternal line. Precordial shock intense and wide. Epigastric beats intense. First sound very muffled, with slight murmur at the apex. Second sound muffled. Pulse very irregular, with frequent extrasystolic lapses. The number of pulsations is more or less 82 per minute. Tmx.=120. Pulse 95, standing. Liver considerably enlarged. Spleen not enlarged. Thyroid enlarged, with voluminous cysts of the lateral lobes. Edema. Bronchitis. Glands enlarged.

After a few days in hospital the patient was discharged as he was much better. He came back on June 5, 1913. Edema. Intense dyspnea after the slightest effort. Nocturnal dyspnea. Frequent palpitation. Heart continues much enlarged. Apex 12,5 cm. from the midsternal line, within the anterior axillary line. Right margin 4,5 cm, from the midsternal line. Precordial shock ample and violent, shaking all the precordium. First sound muffled, second reduplicated, with strong pulmonary accentuation. Cardiac beats very irregular, with slight repeated crises of tachycardia; number of beats varying between 75 and 82 per minute. Tmx.=110. Turgescence of the veins of the neck. (See tracings). Liver much enlarged. Spleen not palpable. Slight improvements only; the treatment was interrupted. We heard that he died in asystole a month after leaving the hospital.

Records nos. 33 nda 33-A.

May 11, 1913.

I) The radial pulse shows beats of the dominant rhythm, their sequence interrupted by extrasystolic cycles. The beats proper of

the dominant rhythm are not perfectly rhythmic, there being variations; the examination of the jugular pulse shows them to arise from different causes.

First of all, the rate of the *a* waves is not regular, sometimes more rapid, sometimes slower. Some waves are so much anticipated that they seen to be rather auricular extrasystoles than beats of the dominant rhythm.

The conduction of the stimulus retarded, and the delay of the conduction also contributes to the arrhythmia. The extrasystoles are generally ventricular. II) Tracing 33-*a* was taken 15 days aftar the anterior one, and does not differ from it substantially. The rate is more rapid and the conduction slower; the *a* waves often fall in the systolic phase of the previous cycle.

The extrasystoles are numerous and of ventricular origin, and in the first part of the tracing an interpolated extrasystole is seen.

Observation no. 35.

Partial block. Rhythm of 2:1 and of 1:1.

J. C. de A., mulatto, male, 28 years old, laborer, married, resident at N. S. da Gloria. Previous history of attacks of malaria nearly every year. Some attacks of bronchitis with chills. He does not mention venereal disease or rheumatism. This patient smokes and takes coffee; formerly he drank spirits, but he has stopped doing so for the last two years. About two years ago he had palpitation, strong rapid and uncomfortable beats and fluttering of the heart. The palpitation came on in attacks sometimes after an emotion and sometimes without any apparent reason. Great irritability and nervous excitability; he cannot stand being with many people; any loud talking, or rapid movements or effort provoke an attack of palpitation. This condition is accompanied by trembling and a sensation of cold; the patient says he feels a ball in his stomach which rises to the chest and throat, stopping his breath and causing agony (avexame). Frequent giddiness without causing him to fall. General weakness. Inability to work. The slightest exertion fatigues him and brings on palpitation and agony (*avexame*). He has good appetite, but the ingestion of food causes uneasiness and abundant eructations. No edema.

Heart enlarged. Apex beat in the fifth space on a level with the mammillary line, 9,5 cm. from the midsternal line. Right edge 4 cm. from the midsternal line. Shock diffuse. Pulse arrhythmic, with frequent pauses which are not extrasystolic. The jugular tracing shows the presence of a wave during the long pauses of the ventricle. Pulse ample, empty, soft, from 43 to 55. Tmx.=125. The number of beats rises to 92 when standing and 100 after exercise. The neck veins are not turgid; the jugular waves are very visible. We proceeded to the atropine test. The analysis of the tracings may be studied. Liver enlarged, painful on pressure. Spleen not palpaple. Thyroid without noticeable enlargement. Inguinal glands slightly increased. Nervous system negative. Intellect normal.

Record no. 34.

I) The radial pulse is arrhythmic, uot only on account of the lapses of the pulse after three or four beats of the dominant cycle, but also because the cycles of the dominant rhythm are not exactly equal. In the venous pulse, *a* waves are seen in regular succession. There is also no ventricular systolic wave in the venous pulse at the points which correspond to the lapses of the radial pulse. The lapses come from the block of auricular waves. Immediately after a blocked wave, the *a c* interval of the following cycles is normal, but it lengthens gradually in the following cycles until a new block occurs; this goes on in succession. The gradual retardation of the ventricular systoles by the changed conductibility explains the variation in the rhythm of the radial pulse.

Record no. 34-A.

II) In the tracing, which was taken half an hour after the injection of a milligram of

atropine, the pulse has become regular, the conductibility being reestablished, The *a c* interval is normal. The pulse was a little accelerated.

Observation no. 36.

Ventricular extrasystoles. Partial block.

T. M. P., 58 years resident at Pilar.

Examined June 2, 1911. Complains of palpitation with continual giddiness. Pulse 59 with frequent lapses. Hypertrophy of the thyroid.

Record no. 35

The pulse is arrhythmic, the arrhythmia being caused by complete lapses and premature beats which interrupt the dominant rhythm irregularly. The cardiac tracing does not furnish any indications that can be used, as the respiratory movements affect it a great deal. The collective analysis of the tracings shows that the lapses of the pulse are caused by the irregular block of auricular waves. Thus between the beat III and IV an *a* wave is seen in the jugular pulse; this wave is seen in the cardiac tracing as well is in the catacrotic wave of beat III, but there is no corresponding ventricular systolic wave. The same is repeated in beat VIII—IX and in other parts of the tracing.

Beat X is premature, as a result of a ventricular extrasystole which falls at the same time as the auricular systole of the dominant rhythm. Other extrasystoles are seen in the tracing, all of them ventricular. The *a* waves appear rhythmically in the jugular pulse, the *a c* interval lengthening slightly and gradually until the block, as may be seen in beats IV to VIII.

Observation no. 37

Partial block. Rhythm 2:1 and 1:1, alternating irregularly. Giddiness.

A. D., negro, male, 27 years old, laborer, married, resident at Piedade.

Has had intermittent fevers for many years. A year ago he had milkpox. Has gonorrhea and venereal chancres. He has been ill for a long time, with an undefined uneasiness, which however did not prevent him from working. Has frequent attacks of giddiness, sometimes vertigo and falls. Rarely has palpitation. Dyspnea on exertion. These symptoms have become worse lately; the last few days he has had edema of face and abdomen. Heart not enlarged. Apex 7 cm. from the midsternal line and right margin 3 cm. Apex beat below and within the nipple. Heart sounds muffled. Pulse ample, strong, arrhythmic and irregular, accompanying the heart beats. Series of frequent beats interrupted by slow series. In the long ventricular diastoles is heard a sound which is probably auricular. Jugular pulse hardly visible. Pulse 56 per minute, varying, however, according to the number of the slow beats. Tmx.=140. Atropine test. (See tracings). Liver, left lobe enlarged. Spleen not palpable. Thyroid enlarged. Inguinal glands not enlarged.

Record no. 36.

The radial tracing shows beats sometimes more rapid; the interval between the systoles of the slow beats is perceptible, but not strictly equal to twice the rapid beats. The cardiac tracing shows, besides the identical rhythm, very clear *a* waves which are followed or not by ventricular systolic waves. The *a* waves which are not accompanied by ventricular systoles correspond to the catacrotic phase of the pulse waves of the slow rhythm. In the jugular tracing are seen *a* waves which succeed each other in regular intervals. They are not all, however, followed by a ventricular systole, some waves being blocked. In the beats I to IV the block occurs in the rhythm of 2:1. The beats V and VI follow in the rhythm 1:1, with gradual increase of the *a c* interval and the rhythm that of partial block; 2:1 reoccurs following the VI beat. The gradual lengthening of the *a c* is marked.

Record no. 36-A

A quarter of an hour after the injection of 0,g 001 of atropine the pulse has become regular, there remaining a perceptible lengthening of *a c* interval. The acceleration of the rhythm is as follows 77: 83.

Observation no. 38.

Partial block. Bi – and trigeminal rhythm.

E. S., male, about 30 years old, Previous history obscure. Cretinised appearance. Mouth half open, with saliva running down at the corners. Defective speech with marked general trembling. Bilateral dysbasia, the patient admitting previous paralytic condition.

Patellar reflex on both sides very much exaggerated. Intellect much below the normal. Liver and spleen much enlarged. Numerous glands in the neck, in the axilla and in the inguinocrural region. Thyroid not noticeably enlarged. Pulse arrhythmic, with bigeminal appearance, sometimes trigeminal, sometimes with beats in regular succession; there appear to be extrasystoles. Pulse lying down 52: standing 57. Tmx.= 135. Signs of cardiac insufficiency; partial fatigue on exertion; giddiness and uncomfortable palpitation which prevent him from. working.

Record no. 37.

The tracing of the heart and pulse have bi – and trigeminal appearance, interrupting a succession of slow beats. This is caused by the partial and irregular block of auricular waves. The auriculo-ventricular rhythm is sometimes 1:1, sometimes 2:1. The slow beats show the rhythm of the block to be 2:1 and 3:1. The origin of some beats, as for instance X, is doubtful; it is perhaps heterogenetic, not depending on *a* 13 as might also be interpreted. The polygraph is not enough to decide this question.

Observation no. 39.

Partial block; irregular rhythm 2:1 and 1:1; Cardiac insufficiency; Sudden death.

G. N., mulatto, male, 40 years old, laborer, married, resident of Burytys. November 11, 1913. Previous history includes attacks of malaria, gonorrhoea and probably syphilis. Does not mention rheumatism. For some time past has suffered from palpitation, rapid, strong and annoying beats, with respiratory difficulty, localized in the precordium and the vessels of the neck, coming on in attacks provoked by emotion or without perceptible cause. Dyspnea on exertion and at night. He is always short of breath. Gastric pains and headaches. This patient has had attacks of intermittent fever and has frequent giddiness.

He is above middle height and of strong constitution.

Intense jaundice; at present he has no edema, nor does he mention any in the past. General trembling, when examined very intense from emotion, afterwards diminishing. Heart much enlarged, apex beat in the fourth space, 13 cm. from the midsternal line. Right margin 6 cm. from the midsternal line. Precordial shock ample, outside the nipple, the third and fourth intercostal spaces retracted in the precordium, First heart sound very muffled, followed by murmur with an area inside apex. Second sound reinforced in the pulmonary area. Rhythm of three beats at apex, the additional tone clearly separated from the first murmur. Pulse slow, irregular, arrhythmic with frequent lapses; the number of beats varies from 52 to 56. In the long pauses of ventricular systoles is heard a shock, and also a sound synchronous with the venous wave of the jugular; auricular systole not transmitted. The beating of the neck veins is clearly seen as also that they are more numerous than those of the pulse; clearly perceived are also the venous waves which coincide with the cardiac sound as well as a slight shock, without ventricular contraction. Tmx.=110. Liver and spleen much enlarged. Thyroid enlarged; has cystic nodules.

November 13, 1912. After resting and treatment this patient got much better. All his symptoms diminished. Cardiac area per

ceptibly reduced. Apex at 10,5 cm. from the midsternal line and right margin at 4,5 cm. The pulse remained irregular. Sometimes longer and sometimes shorter pauses. Num ber of beats varying from 50 to 52. The atropine test regulated the pulse, as is seen in the tracings, though there appeared rare occasional extrasystoles. Liver and spleen still enlarged. We did not see the patient any more, but heard that he died suddenly in July, 1913.

Records no. 38 and 38A.

These tracings were taken on successive days and show the same characteristics.

The radial pulse shows occasional, perceptibly rhythmic, beats, whose sequence is interrupted by shorter cycles, which appear irregularly. The cycles of long pauses are twice less than those of short pauses. All the heart-beats are amply represented in the radial pulse.

In the venous pulse the auricular waves are rhythmic and more frequent than the ventricular ones; not all the auricular waves are followed by the corresponding ventricular wave. Thus *a* I and *a* III are blocked, not being accompanied by ventricular systolic wave. *a* II corresponds to radial beat I with the *a c* interval lengthened with retarded conduction of the stimulus.

In the radial beats 2 to 3 and 4 to 5 the *a* waves are successively accompanied by ventricular *c* waves, with the *ac* interval gradually lengthening from one cycle to another.

Collectively the tracing registers a partial block in rhythm 2:1, with irregular return to rhythm 1:1.

The tracings 38 b, 38 c, and 38 d show the action of 0g 00075 of atropine.

In tracing III may be seen extrasystolic beats with complete compensating period of rest. They are ventricular extrasystolic beats. The stimulus is conducted through all the auricular waves but the *a c* interval is lengthened.

In tracings 38 c and 38 d the pulse is perfectly rhythmic, but the lengthening of *a c* continues.

The elective action of atropine on the conductibility must be noticed, and there is no perceptible acceleration of the auricular beats.

Observation no. 40.

Partial block.

J. S., male, 11 years, white, resident at Lassance.

First consultation March 3, 1913. Born at term; normal development. Family history obscure. Former illness: repeated attacks of malaria. This patient complained of fatigue and general weakness. Skin discolored and slight general edema. His face was swollen with marked subpalpebral infiltration; base of the thorax enlarged; abdomen flaccid aud voluminous. Liver enlarged, passing the costal margin by two fingers and measuring 11 cm. in the mammillary line; the edge sharp and hard and not painful on pressure. Spleen enlarged and hardened. Epigastrium prominent with marked gastric tympanism. Thyroid enlarged. Cervical and inguinal glands enlarged. Bronchitis of the larger bronchial tubes diminishing. Nothing noteworthy in nervous system. Circulatory system: Heart enlarged, apex beat in the fifth spsce outside the mammillary line, 9 cm. from the midsternal line; right margin 4 cm. from the midsternal line; upper margin reaching the second rib. Arrhythmic beats, with frequent lapses; no sounds to be heard during the lapses. The first sound not perceptibly changed except that it is slightly muffled. Mesosystolic murmur at apex, musical, not propagated. Second sound reduplicated, with pulmonary reinforcement. Number of beats lying down 82; standing 118. Tmx.=105. Katzenstein: before compression of the femorals 82 beats; arterial tension 105; during compression 86 beats; tension 105; after 82 beats. An injection of 3/4 of a milligram of neutral sulphate of atropine produced the following modifications; 104 beats per min

ute; the pulse became regular one hour after the injection; arterial tension unchanged. The analysis of the tracing shows the details of the arrhythmia, and the influence of atropine on the cardiac rhythm. Progress of disease: on the day following the first examination gave 70 beats lying down, and 60 standing, as the lapses were more frequent in the latter position. Pills of quinine and belladonna were prescribed.

5, 3, 1913.

Infiltration considerably diminished, abdomen less voluminous. Arrhythmia persisting and mesosystolic murmur at apex is audible when the patient is lying down, and not when standing.

6, 3, 1913.

Standing 87 beats; lying on his back 76. General condition much improved.

7, 3, 1913.

Size of heart diminished; apex a little below and outside the mammillary line, 7,5 cm. from the midsternal line. Right margin 3,5 cm. from the midsternal line. Beats 85 lying down, the pulse ample, regular and rhythmic. Liver measuring 10,5 cm. at the mammillary line. Spleen unchanged. Stomach dilated, prominent in the epigastric region. The patient took the medicine referred to on the third, fourth, and sixth.

23, 3, 1913.

General condition of the patient much improved so that he can run about 200 meters without fatigue. Size of heart diminished; transverse diameter 10,5 cm. Number of beats lying down 96; standing 124: pulse arrhythmic, with frequent lapses. Tmx.=110. The patient was not seen for a month and a half and only returned on the fifth of June, 1913. His general condition was good, and he no longer had fatigue or edema. Heart-Apex in fourth intercostal space on a level with the mammillary line. 7,5 cm. from the midsternal line. Right margin 3,5 cm. First sound slightly muffled; mesosystolic murmur at apex. Pulse regular and arrhythmic. Beats lying down 70; standing 82; after exercise 96; decreasing rapidly to 82. The patient was re-examined in January 1919, about six years later. He had signs of slight cardiac insufficiency, dyspnea on exertion, acceleration of the pulse after slight exercise and change of position. Heart enlarged, apex beat outside the mammillary line. Precordial shock wide and somewhat violent. First heart sound slightly muffled and lengthened. No murmur. Pulse rhythmic, with no discordancy between the cardiac and radial beats. The enlargement of the heart was confirmed by an X-ray examination made by Dr. R. Duque-Estrada.

Record no. 39.

The radial pulse and heart tracing show frequent lapses which correspond to each other; they appear irregularly, sometimes alternately, sometimes after two or three beats, followed by the dominant rhythm. These also do not occur in perfectly equal cycles. In the venous pulse the *a* waves are at a rapid rate, 115 per minute and rhythmic. The *a c* interval is variable, augmenting gradually after every lapse of the pulse, as may be seen more clearly from *a* XXI *c* ouwards. The lapses of the pulse are due to the irregular block of the auricular waves.

Record no. 39-A, 39-B, 39-C, 39-D, 39-E, 39-F. II, III, IV, V, IV

Show the effect of half a milligram of atropine. In tracing II there is nothing note worthy, besides what has already been said of I, except that the rate of the auricular wave beats is less rapid.

Record no. 39-B (III).

Taken 20 minutes after the injection of atropine shows that the rhythm of the radial beats is already reestablished, and the *a c* interval is normal. Acceleration of the beats is minimal, 103 to 109, and the action of the atropine on the conductibility lasted an hour, although it is to be noticed that the rate is slower, 103 to 100.

Record no. 39-F (VI).

Shows that the effect of the atropine on the conductibility is diminishing; the *a c*

interval is already much lengthened, being equal to four tenths of a second. On the other hand, the rate is much less than before the injection of atropine, 92 to 103. The conductibility is kept in good condition by the use of belladonna with the rate comparatively slow: 85 beats per minute.

Record no 39-H (VIII).

Shows a return to the former state of partial block, with varying lapses in the conduction. The patient had left off taking belladonna some days before this tracing was taken.

Record no. 39-I (IX).

Taken about six weeks after the last; this tracing is quite normal: rhythmic beats; conductibility reestablished as indicated by an *a c* interval of normal length.

Record 39-J (X).

This tracing was taken six years after the preceding one. The pulse is perfectly rhythmic, the restored conductibility continues. Compression of the eye-balls retards the cardiac beats very much and remains after the compression has ceased. The *a c* interval is normal even after ocular compression.

Observation no. 41.

Partial block. Rhythm 2:1.

M. P. F., mulatto, male, 30 years old, laborer, single, resident at Andrade Quicé.

Examined May 4, 1913. The patient had always been well until about two years ago when his present illness began. Fatigue and palpitation with heavy heart thumps. He had edema which disappeared. Some two years ago the patient had malaria. A few days before he came to consult us he had caught cold and had catarrh in the nose and bronchi at the time of examination. Liver and spleen much enlarged and painful on pressure. Thyroid very much enlarged. Glands generally enlarged. Heart much increased in size. Apex 12 cm. outside the midsternal line; right margin 4 cm. Precordial shock large being perceptible in the third, fourth, fifth and sixth. Apex in the sixth space, and passes the mammillary line by 2,5 cm. First sound lengthened and muffled. Mesosystolic murmur, not propagated. Second sound tympanitic and accentuated in the pulmonary area. Pulse ample, full and slow. Beats of the neck veins very easily visible, twice more rapid than the radial pulse. Atropine test. (See records).

May 5, 1913.

Yesterday's examination was made after a long journey and an attack of malaria. After a rest and quinine.

Heart perceptibly diminished in size. Apex in the fifth space, a little outside and below the nipple, 11,5 cm. from the midsternal line. First sound clearer, with inconstant murmur when lying down, which disappears when the patient is standing. Number of beats lying down 70; standing 40;. When standing, the beats are regular and slower; during the long pauses there are auricular contractions to be heard. After the patient has been standing for some time they become irregular; there appear rapid and slower series in succession. Number of beats variable, ranging from 66 to 82.

This takes away the value of the Katzenstein test, during which the following interesting fact was noticed; at the beginning of the compression of the femorals the heart became perceptibly dilated; apex beat in the sixth space. When the compression was continued for five minutes, it returned to the fifth space as before compression.

Record no. 40.

Partial block. Ventricular and nodal extrasystole. The venous tracing shows rhythmic *a* waves at a rate of 107 per minute. The *c* waves follow each other alternately after each *a* wave, the *a c* interval lengthened. The retarding of the ventricular systole thus caused, and the frequency of the auricular rhythm, make the *a* waves fall alternately in the refractory phase of the former systole, so that they are blocked.

The block is consequently in 2:1 rhythm. In some cycles, for example in F, the rhythm returns to 1:1 with the *a c* interval much lengthened.

The beats of cycle P are probably extrasystolic and of ventricular origin.

Record no. 40-A (II).

The injection of 1 milligram of atropine did not improve the conductibility; the block persists in 2:1 rhythm.

Record no. 40-B (III).

The auricular rate has become slower — 84 instead of 107 beats; conductibility improved, cycles of 1;1 rhythm with *a c* interval much lengthened. At some points the block reappears in 2:1 rhythm. Some beats, such as those of cycle XIII, are frankly extrasystolic and of nodal origin, both the auricular and ventricular beats being premature. On the heart tracing the auricular waves are seen very clearly.

Observation no. 42.

Partial block 2:1. Cardiac insufficiency. Sudden death.

M. D. M., white, male, 52 years, married, resident at Porto Manga.

Examined October 14, 1912. Previous history. The patient mentioned attacks of malaria and venereal chancres, but not rheumatism. He has been ill for about 12 years with fatigue, edema and sensation of gastric distension. He has had no attacks, or palpitation, either now or before, and is a well-grown man of robust constitution. Very marked paleness; general edema, more marked in face and lower limbs. Coughs and has dyspnea on exertion. Feels no discomfort when lying down. Frequent giddiness. Heart enlarged, apex beat in the fifth space 11,5 cm. from the midsternal line. Right margin 3,5 cm. from the midsternal line. Base: 15 cm.; height 8 cm. First sound preceded by a sound and substituted by a prolonged murmur during the whole systole, propagated towards the axillary line and not audible at the back. Second sound clear. In the middle of the ventricular diastole is heard a tone accompanied by a slight shock with venous wave in the veins of the neck. These and those of the arms and thorax are turgid. Pulse 36, not varying or only very slightly in different positions. 37. Tmx.=160. The atropine test produced a slight modifcation of pulse, as can be seen in tracings. Liver and spleen very much enlarged with moderate goiter.

This patient stayed three days in Lassance and returned afterwards to his home, three leagues away. On arriving he died suddenly.

Record no. 41.

October 14, 1912.

This is a tracing of partial block. There are three very clear waves to be seen in the jugular tracing; 2 of them form an *a c* group which is repeated in regular periods of 17 tenths; the *a c* interval is variable; sometimes there are 2 tenths, sometimes slightly more or even 3. In the midst of each interval between 2 *a c* groups appears an *a'* wave which is not transmitted to the ventricle so that the ventricle beats just twice less often than the auricles. The V wave is slightly marked and in some places does not even show. At some points the wave V is however clear so that it can be marked precisely. The seventh and eighth beats of the tracing show rather anomalous intervals. The seventh is shorter and the ninth longer; one might suggest an extrasystole followed by a compensating period of rest. The analysis of the jugular pulse shows, however, that it is really a variation in the time of production of the stimulus. The auricular waves appear clearly in regular succession; they are slightly accelerated in group 7 and retarded in group 8. Tracing 3a taken 20' after injection of 1,g001 of atropine shows nothing noteworthy except that the atropine has had no influence either on the auricular or ventricular beats. This has also been noticed by some authors without a satisfactory explanation. In tracing IV taken 80

minutes after the atropine injection there is some improvement in the conductibility; there appear 2 beats in 1:1 rhythm. It is remarkable that far from the auricular rhythm being accelerated, it is on the contrary slackened, 70: 65.

Observation no. 43.

Partial block, 1, 2, 3. Agony. (avexame).

I. N. C., mulatto, male, 20 years old, laborer, single, resident at Jatobá.

About ten years ago he had intermittent fevers aud mentions nothing else. This patient has had fatigue, pains in the legs, pain in hypochondrium, attacks of palpitation with very rapid precordial beat accompanied by agony. Giddiness, especially when getting up. He does not mention attacks. Has had edema but not at the time of examination.

Under-sized individual. Marked paleness. Heart enlarged. Apex in fourth space in the mammillary line. Right margin 4 cm. from the midsternal line. Precordial shock diffuse and strong, shock double as if reduplicated in the pulmonary area. First sound prolonged, weak, without murmur. Second sound reduplicated and accentuated in the pulmonary area. Mesosystolic murmur in the pulmonary area. Pulse irregular, arrhythmic and very variable. Sometimes slow, about 50 beats, sometimes rapid, with extrasystoles chiefly brought on by emotion. Number of beats lying down 52; standing 62; after exercise 66. Beat of neck-veins very clear with more waves than the radial pulse. In the ventricular pauses is heard a muffled tone of auricular contraction which is not transmitted.

Katzenstein { Before – 65 Tmx. 135. During - 68 Tmx. 145. After – 54

When standing the number of pulsations rises to 76, and after exercise to 84.

Liver not enlarged. Spleen enlarged. Marked gastric dilatation. Thyroid much enlarged. Inguinal and epitrochlear glands slightly enlarged.

Records nos. 42 and 42-A.

The tracings are identical, varying only as to the velocity of the record.

The tracings of heart and pulse are analogous and show irregular and arrhythmic beats, the origin of which can be traced by the analysis of the jugular pulse. Here the *a* waves are seen succeeding each other very frequently; some of them are blocked. The block is irregular, sometimes in the proportion of 2:1, sometimes 3:1. At some points, as at beat XI, it is difficult to decide whether the rhythm has returned to 1;1 with a greater lengthening of the *a c* interval or whether the beat is extrasystolic.

Observation no. 44.

Partial block. Stokes-Adams' syndrome. Harmful action of digitalis.

A. A. C., male, 39 years, resident at Curvelo.

Examined December 12, 1914.

The patient dose not mention lues nor are there any signs of it. He has had palpitations now for four years, and for the last two has had passing giddiness. About one month ago he had giddiness causing him to fall and lose consciousness; the giddiness lasts for some seconds but occurs rarely. After the use of digitalis had giddiness more often.

Pulse slow, 34 radial pulsations to the minute. Sometimes cardiac bigeminism, the second beat not being perceptible in the pulse. Cardiac area frankly increased.

Liver enlarged.

This patient came back to consult us six weeks after the first examination. He has had no more giddness. Pulse more rapid, 60 beats. There are lapses in the radial pulse which correspond to long cardiac diastoles in which a tone, problably of blocked auricular systole, is heard. In the in-

terval between the two examinations the patient stopped taking digitalis.

Record no. 43.

The radial pulse is irregular and arrhythmic. In the jugular tracing the *a* waves follow one another regularly but are irregularly blocked, sometimes with rhythm 2:1, and sometimes with 3:1.

Observation no. 45.

Total block. Stokes-Adams' syndrome.

M. A. L., male, 54 years of age, resident at Curvelo.

Examined October 22, 1914. Previous history unclear; no sure indication of syphilitic infection, of which there are no traces. The patient complains of epigastric anxiety, sensation of oppression and vague pains in the precordial region. For seven months he has had attacks of giddiness for a minute or more, without convulsions, brought on by a short run or any other effort, sometimes coming on at short intervals for some hours on stretch. Copulation always brings on these attacks. Abundant eructation with aerophagy. Pulse slow, 32 beats, lying down or standing. Cardiac auscultation during the long pause reveals a short tone of blocked auricular contraction at varying intervals from the cardiac systoles.

Record no. 44.

The radial pulse accompanies the cardiac tracing in slow beat—32 a minute. The waves are regular and rhythmic. The venous tracing shows more frequent auricular waves, 65 per minute, but not in constant relationship to the ventricular systolic waves. The block is total, the ventricle following its own rhythm.

Observation no. 46.

Total block. Stokes-Adams' syndrome.

J. O., male, white, 12 years, resident at Gustave de Silveira.

Examined July 9, 1912.

Family history: Mother strong, 45 years old; father died suddenly; he suffered from heart trouble. Eleven brothers and sisters alive and strong; one brother died at the age of three and one was still-born. Personal history; the patient was strong until seven months ago and does not mention having had any illness until then. About seven months ago he began to have dyspnea on exertion, at first only when he had to walk far and fast; now he has it even when he walks slowly on flat ground. Weakness in the legs. Giddiness. No edema. Has had fainting fits and loss of memory, sometimes with convulsions.

The boy is well developed, pale and has myxedema in a slight degree. No edema. Heart enlarged; apex beat in fifth space, 9 cm. from the midsternal line. Sounds quite audible. First sound is accompanied by musical systolic murmur within the apex not propagated. Second sound reduplicated and reinforced in the aortic area; at times an isolated tone of auricular systole, which is not transmitted, is to be heard at the ventricular diastole, 37-38 a minute. Liver enlarged. Spleen not enlarged. Thyroid enlarged. Nervous system negative. Respiratory system negative.

July 19, 1912.

Between the two examinations the patient had three attacks. Slight edema of face and limbs. Pulse 37; physical condition of the heart unchanged.

Record no. 45.

A classic total-block tracing. The radial waves and the apex beats succeed each other rhythmically; pulse slow; 37. In the jugular tracing the *c* waves show no stable relation to the *a* waves; they are more numerous, 100 per minute. The *a* waves succeed each other rhythmically; sometimes they are elevated, at others less marked, according to whether they do or do not fall within the ventricular systolic period. C. V. (E interval). No atropine test.

Observation no. 47.

Total block. Stokes-Adams' syndrome.

P. C. G., male, white, 18 years old, resident at Morro da Garça.

The patient says he had ill-defined attacks when a child; he has frequent attacks of giddiness and about six months ago convulsions. Six months ago he had milk-pox. Complains of gastric pains with sensation of weight in the stomach. Intestinal functions normal. Liver enlarged and painless. Spleen slightly painful and enlarged. Heart much enlarged, measuring 16 cm. at base. No murmur, but after each normal systole is heard a muscular sound, apparently due to the contraction of the auricle, which is iregularly heard. Pulse arrhythmic; slow; sometimes there seem to be extrasystolic waves. 36 pulsations a minute. Tmx.= 135. Pulse lying down 36; standing 44.

Record no. 46.

July 5, 1911. Pulse slow and rhythmic, 34. Cardiogram more frequent than the pulse, not full, with the auricular waves well marked in the diastolic phase and falling at varying distances from the ventricular systoles. The jugular tracing shows the *c* waves placed in varying relations to *a*, there being no dependence upon the latter. The *a a* waves are frequent and rhythmic, 93 per minute. The *v* waves show nothing noteworthy. It is a record of easily interpreted complete block.

Observation no. 48.

Ventricular extrasystole evolving towards complete block.

J. C. F. R., male, white, 17 years old, native of Lassance. This patient, who has a goiter with a generalized enlarged thyroid, came to the Hospital for the first time in May, 1911. He had slight indications of cardiac insufficiency and extrasystolic arrhythmia. In January, 1915, about four years later, he came back to consult in an asystolic crisis, with slow and arrhythmic pulse The asystolic symptoms were improved, the edema disappeared, but the arrhythmia remained, with slow pulse. Heart much enlarged. No murmur, or valvular lesions.

Records no. 47 and 47-A.

The records show the evolution of the arrhythmia which is wholly extrasystolic in the first record, and three years and a half afterwards has become a complete block with extrasystoles.

I) The collective record rhythmic, the dominant rhythm interrupted by premature beats of ventricular origin, with complete compensating period. *a c* interval not lengthened. Nothing else worth mentioning.

II) Taken three years and a half after the former.

The radial pulse is slow and irregular; there are a few extrasystolic beats. The cardiac record is defective, and furnishes few data. In the jugular record *a* waves are seen succeeding each other regularly and much more numerous than the ventricular beats *c* waves. The relation between *a* and *c* varies every moment; at times they fall together, at others *a* comes before *c* in varying time, sometimes it comes after *a*. The *c* waves of the ventricular extrasystole interrupt the succession of *a* and *c* which are regular, without any accidental connection which might be attributed to the auricular waves. The record is of complete block, with ventricular extrasystoles.

Observation no. 49.

Alteration of conductibility with extrasystole. Evolution of morbid process till complete block.

M. F., male, 23 years old, white, resident at Lassance.

He came to consult us stating that periodically he has vertiginous crises with loss of consciousness. Previous history unknown. Lives in a house infestedby *Triatoma*. Family history: His parents had extrasystolic arrhythmia and hypertrophy of thyroid gland. Three brothers with goiter and al-

ternation in the functioning of the heart. One brother with goiter, extrasystolic arrhythmia and cardiac insufficiency. Four daughters with signs of *trypanosomiasis*. Wife of healthy appearance, has had no miscarriages.

At time of examination: Robust appearance, below medium height, well-proportioned, muscular. Hypertrophy of thyroid gland. Liver and spleen enlarged. No edema. Extrasystolic arrhythmia. In this phase the extrasystoles were frequent after groups of five, six or seven normal systoles.

April 9, 1910.

Cardiac pulsations 62; radial 45. The patient only came back to consult us on the 22nd of November; he had rare extrasystoles, evident alterations of conductibility; pulse lying on his back 48; standing 45.

At present no crises of giddiness.

February 7, 1911.

The alterations of conductibility are very distinct. Pulse 44. The patient was not seen, again until 1913, when he came back on the fifth of March with the following symptoms: Dyspnéa on exertion and when lying down so that he can only rest propped up. Nocturnal dyspnea marked. General weakness, no giddiness, nor vertiginous crises. Appetite good. Liver enlarged and painful on pressure in the epigastric region. Spleen slightly enlarged. Heart: apex in sixth space, below and outside the nipple, 11 cm. outside the midsternal line. Right margin 5 cm. outside the midsternal line. Precordial shock ample, with perceptible beats in fifth and sixth intercostal spaces. First sound very muffled. accompanied by inconstant murmur in the strong beats, with slight propagation towards the axilla. In the long intervals after the second sound are heard short slight tones without repercussion on the radial pulse, coinciding with the rises of the neck veins. The second sound reduplicated with pulmonary accentuation, muffled in the aortic area. Pulse ample, slow and regular. Extrasystoles at long intervals. Forty-two beats. Venous pulse very clear.

Like the cardiac beats, it shows that there is complete disconnection between the auriculo-ventricular beats.

May of the same year.

Condition of the heart the same. Liver diminished. Subjective signs much better.

July of same year.

Fatigue on exertion and walking. The patient sleeps well and has no dyspnea at night or when lying down; some attacks of giddiness. Examination of heart: Apex in the sixth space a little outside the mammillary line and 10 cm. from the midsternal line. Shock but slightly perceptible. Right margin 4 cm. from the midsternal line. First sound muffled but with irregular tone, sometimes being much higher and more intense. Auricular tone audible in different phases of diastole, sometimes nearer and sometimes further from the next ventricular systole. The coincidence of the auricular and ventricular beats seems to explain the greater intensity of the sound at times. Pulse: lying down 42; standing 46, Tmx.=135. Liver slightly enlarged, painless. Thyroid perceptibily enlarged.

September 9, 1913.

Dyspnea on exertion, even when walking normally at ordinary pace and on even ground, much worse when he goes uphill. No nocturnal dyspnea. Heart much enlarged, first sound lengthened and muffled. Second sound also muffled, sometimes reduplicated. The auricular beats are also heard well and are not followed by ventricular contractions. 40 beats with a few extrasystoles. Terminal phase: The patient was not seen for some months. In May, 1914, he came back in asystole with general edema, dyspnea, congestion of the bases of the lungs, turgid neck veins, liver enlarged, etc. Heart greatly enlarged with dilatation of all the cavities. He died at home in this state, and a post-mortem was not made.

Records no. 48, 48-A, 48-B, 49-C, 48-D.

These tracings show the evolution of alteration of the rhythm from extrasystole to complete block.

I) Radial record, on the right side, in which is seen the dominant rhythm is rapid, 100 a minute.

In this record are seen slow beats occupying the space of two cycles of the dominant rhythm; they are probably due to extrasystoles which are not represented in the radial pulse. At some points they are shown by slight beats. The third beat is succeeded by two consecutive extrasystoles.

II) Taken about six months after the first; radial record similar to the cardiac one, slow beats interrupted in their succession by cycles of shorter diastolic phases. The long diastolic phases are perceptibiy twice as long as the short ones.

In the cardiac record small waves of auricular contraction are to be seen in the long diastolic phase, but none of ventricular systole.

In the jugular pulse the *a* waves are marked rhythmically. They do not however all have a corresponding ventricular wave as many are blocked. The block is in 2:1 rhythm corresponding to the slower ventricular beats and returns to 1: 1 in the rapid ventricular beats. The *a c* intervals, where the rhythm is 1: 1, as in cycle XIX, perceptibly lengthened.

III) About two years later; the tracing is already that of complete block. The ventricles beat regularly at the rate of 40 per minute; nothing noteworthy in the radial and cardiac tracings.

In the phlebogram are to be seen auricular waves at an accelerated rate of 100 per minute; there is no constant relation between the auricular and ventricular rhythms.

IV) After an injection of 0,001 g. atropine there was no change in the relation between the auricles and ventricles, nor in the cadence. There appeared however a ventricular extrasystole at the left of the tracing.

V) Tracing taken little more than a year later, during an asystolic crisis. Auricular waves in the venous pulse show increased rate, 120 per minute. *A* and *c* waves completely independent. On the left side of the tracing the ventricular beats marked in the radial pulse and in the cardiogram; they are rhythmic and at a rate of 40 per minute. On the right side they are irregular, with numerous extrasystolic beats. The patient complained of umcomfortable heart-beatings at the time.

Observation no. 50.

Total block.

J. M. S., mulatto, male, 38 years old, widower, laborer, resident at Areias. (near Curvello).

Examined June 26, 1913. Previous history only intermittent fevers. He has been ill for about three months. Until then he worked regularly without fatigue. At the time he had violent giddiness, with darkened field of vision, but without loss of consciousness or fall. This giddiness did not return but there appeared dyspnea on exertion, and agony with weight in the stomach. Lack of appetite; the taking of food in even small quantities often provoked a feeling of fulness, anxiety and fatigue. These symptoms became gradually worse, and lately he has had dyspnea when lying down and at night, preventing him from sleeping, and also edema of lower extremities. Does not complain of palpitation, and does not feel the heart beats. The patient is of medium height, well built and robust.

At present edema of the lower extremities, neck veins turgid. Abdomen distended. Dyspnea on lying down so that the patient cannot occupy a horizontal position. Very emotional, much impressed by the examination. Heart much enlarged. Apex beat in the sixth intercostal space, between the mammillary and axillary lines. Right margin 4 cm. from the midsternal line. Transverse diameter 15,5 cm. Precordial area very prominent. Precordial shock slow, diffuse and undulated. First sound muffled and lengthened. Second sound reduplicate, with pulmonary accentuation. No murmur. Beats arrhythmic with extrasystoles and long pauses. During the long paus-

es sometimes a muffled sound to be heard; it coincides with wave in the veins of the neck and not to a ventricular contraction; an auricular contraction sound. During the examination numerous extrasystoles occurred, almost all of them not shown in the radial pulse. Heart bearts 59. Pulse 36.

Katzenstein { before – 59 Tmx. 160 / during – 66 Tmx. 160 / after – 69

The extrasystoles were probably due to the strong emotion brought on by the examination. Liver enlarged and painful on pressure. Spleen also (Previous malaria). Thyroid enlarged, with large goiter.

Examined June 27, 1913. Patient calmer. Occasional extrasystoles. Auricular sound very audible. Pulse varying between 32 to 35. Standing: 40.

Katzenstein { Before – 36 Tmx. 168. / During—44. / After 44.

The increasing of the beats after compression of the femorals is due to the numerous extrasystoles. Atropine test: While the effect lasted the pulse became regular. Iliac compression hardly alters the number of beats.

Before compression: 36
During " : 36

It is interesting to note that emotion and compression of the femorals brings on extrasystoles.

Record no. 49.

February 27, 1913.

Pulse interrupted by a beat of a lesser cycle followed by the dominant rhythm. The cardiac record shows the same succession of beats with the same rhythmic cycle of 9, interrupted by a lesser one of 6. In the diastolic phase are seen diastolic rises corresponding to the rises of the jugular record. Jugular record with a series of rises of equal cycles not in constant relation to the *c* waves; some are not accompanied by ventricular contraction. They are *p* waves which are not transmitted to the ventricle. Total block.

Taken 35 minutes after 0,001g atropine.

The number of ventricular beats has not changed much; 34:35. The number of auricular beats diminished 100:76. The independence between auricular and ventricular contractions continues.

Observation no. 51.

Complete block. Sudden death.

A. F. C., male, white, 29 years, old, laborer, married, resident at Maquiné.

Previous history: attacks of intermittent fever and gonorrhea some years before. Has been feeling ill for about a year, fatigue on exertion, cannot walk fast, nor go up-hill, as he is so easily tired. He could however do ordinary farm work. About five months ago he became considerably worse, fatigue increased, his stomach seemed to have swelled and has pains like a belt round his stomach and gastro-intestinal pneumatosis. The dyspnea has become gradually worse and comes on after the slightest effort or even when at rest, specially when lying down and at night, so that he can only sleep propped up. At times cannot sleep at all on account of nocturnal dyspnea and cough. Lately, he has had edema of lower limbs, which afterwards extended. Palpitation with uncomfortable heart beats. Has an uncomfortable feeling on account of the extrasystoles which he says *"makes his heart beat twice in one beat"* and is accompanied by uncomfortable feeling of fatigue. At times he feels rapid, strong and very uncomfortable beats.

Present condition, general edema. Dyspnea which gets worse after the slightest effort or when lying down.

Turgidity of neck veins with well-marked pulsation. Prominent swelling of the precordial region. The area of cardiac dulness very much increased. Apex beat in sixth space, beyond the anterior axillary line, 18 cm. from the midsternal line. Pre-

cordial shock ample and slow. First sound lengthened and muffled, substituted in the tricuspid area by a systolic murmur which is hardly audible at the apex. Second sound muffled in the pulmonary and aortic areas. Cardiac rate slow, 48. At the beginning of the examination there were numerous extrasystoles which became rarer in the course of examination. Beats of the neck veins more frequent than the ventricular systoles. Venous pulse positive with systolic thrill in the veins at the right side of the neck, In the intervals of the ventricular systoles, at times an isolated tone is heard; it is synchronous with the venous wave of the jugular. without ventricular contraction. at times producing a slight diastolic impulse; isolated systoles of the auricles. Pulse irregular and arrhythmic on account of the extrasystoles which are sometimes perceptible in the jugular pulse and at others not. Liver enlarged. Slight peritoneal effusion. Bronchopulmonary edema. Thyroid enlarged, principally the right lobe.

October 31, 1913.

Improvement of all the symptoms, both subjective and objective. Dyspnea decreased, as also paltitation and edema. The patient still feels his heat *"beat twice in one stroke"*. No more tricuspid murmur. Area of dulness much diminished: apex 12,5 cm. from the midsternal line; right margin 5,5 cm. Cardiac beats irregular and arrhythmic with frequent extrasystoles; 47 beats per minute, but the number varies according as to whether there are more or fewer extrasystoles.

November 3, 1913.

Improvement continues. Ascites diminished, though not entirely gone. Slight edema of body. Cardiac dulness not modified in relation to last examination.

Tricuspid murmur again to be heard. Heart beats 33, 44, or 46 according to the number of extrasystoles. At beginning of examination extrasystoles in bigeminal series.

November 5, 1913.

Improvement more marked. No more tricuspid murmur. Heart area reduced, principally at the right side. Cardiac beats slow and regular.

November 6, 1913.

Improvement. Cardiac area reduced; apex 11.5 cm. from the midsternal line; right margin 4 cm. from the same. Cardiac beats regular and slow. Sounds more distinct. No murmur. Neck veins no longer turgid. Extrasystoles, sometimes in bigeminal series. 50 beats. The reduplication of the first and second sounds clearly heard, the latter with pulmonary reinforcement. Palpitation rare.

November 10, 1913.

After a relapse brought on by neglect of treatment, the patient improved again. He was not observed for about two months.

Examined January 12, 1913.

Condition like at the last examination with symptoms of asystole. Number of beats varies around 50, according to the greater or lesser frequency of extrasystoles.

January 16, 1916.

General condition improved without reduction of the area of dulness. Number of beats: 46 per minute. On the 20th when going to the Hospital, he died suddenly. A histopathologic examination of the heart was made by Professor B. C. Crowell who confirmed the existence of the lesions characteristic of Chagas' disease, which he has described in his paper on the subject.

Record no. 50.

The beats of the cardiac and pulse tracing show a slow rate with some extrasystolic beats, which are not all marked on the latter, producing long pauses of the pulse. The extrasystoles are ventricular as is shown by the venous record. In this the *a* waves are seen completely dissociated from the *c* waves. It is a case of complete block with frequent extrasystoles which the patient felt as uncomfortable beats.

Records no. 50-A, 50-B.

They show that atropine had no influence on the conductibility, accelerating the auricular beats slightly. The ventricular rate slower owing to the lesser number of extrasystoles.

Observation no. 52.

Complete block. Stokes-Adams' syndrome.

I. F., mulatto, female, 20 years, single, resident at Bananal, near Lassance.

Less than average height. Earthen paleness. Cretin-like appearance with slight exophthalmia. No noticeable asymmetry of face. Complains of fatigue, giving way of legs, general trembling which prevents her from working. Strong, measured heart beats, bringing on agony, a feeling of oppression, agony in the chest and the throat. Almost constant feeling of depression and discouragement with weeping fits without any real cause. She has had giddiness and vertigo, sometimes with loss of consciousness. Constant uncalled-for sadness, always agony; general limpness. During the examination, the emotion brought on an attack of strong and uncomfortable beats. The rate and rhythm of the beats, however, did not differ from those observed at other times. Dyspnea on exertion and when lying down. She has been ill for a long time, having grown worse in the last three months.

Does not mention edema before, nor has she any at present.

Heart much enlarged, apex beat in the sixth space at the level of the anterior axillary line. Right margin 4,5 cm. from the midsternal line. Transverse diameter 16,5 cm. Precordial shock strong and diffuse. First sound lengthened and accompanied by murmur audible in the whole of the cardiac area, with slight propagation towards the axilla. Second sound reduplicated. Pulse slow and ample, the number of beats varies from one moment to another, oscillating between 27 and 32. Different polygraphic records were taken. The atropine test was also made and did not increase the number of pulse beats. Liver enlarged, painful on pressure. Spleen slightly enlarged (previous history includes malaria). No marked digestive trouble. Appetite good; digestion good; does not complain of indigestion. Thyroid enlarged, with large goiter. Regular menstruation at right time, scanty, accompanied by abdominal pains and colics, general condition being much worse at such times. Feeble intellect. Apathetic. Uneasy and uncertain movements. Patellar reflexes slightly exaggerated. During the two and half months in which the patient was under observation there was little change in her condition. The "agony" continued and also the inability to work, frequent fits of weeping, undefined and constant sadness. Sleeplessness. Profuse perspiration especially of hands and feet. Cardiac area unchanged. Pulse varying between 27 and 36.

Examined March 7, 1911.

Complains of general indisposition, headache, profuse perspiration, pains in her legs, giddiness even when lying down; all these symptoms have become worse in the last few days. On the day of examination she had bilious vomiting with marked epigastric feeling of anxiety. Icterus. Furry tongue, with constant bitter taste. The patient complains of heat although the temperature does not rise above 36,8. Rapid emaciation in the last few days. No perceptible change in heart as compared to the result of former examinations. Cardiac area not modified. Pulse, 32 beats. Liver enlarged, but not very much. Urine: no albumen. Abundant bile pigments. This state with a slight change for the worse until ninth. From the ninth to the tenth frequent convulsions came on with loss of consciousness. Pulse feeble, oscillating betwenn 25 and 28. Superficial respiration interrupted by deep sighs. The attack came on at ever shorter intervals, the patient comatose, the coma lasting for about twelve hours During the coma the pulse was irregular, sometimes slower, sometimes more rapid, at times very slow with pauses of from 10 to 15 seconds.

Convulsions, fits of agitation, with intervals of rest. Death followed from heart-failure. A histopathologic examination of the heart was made by Professor Crowell, this being one of the cases which he has used for his description of the specific lesions of the heart in the chronic form of Chagas' disease.

Record no. 51

Pulse and cardiac tracing slow, 32 beats. The phlebogram shows that the *a* waves appear more frequently than the *c* waves, without keeping up constant relations. Total auriculo-ventricular disconnection.

Record no. 51-A.

The disconnection persistent The injection of atropine half an hour previously did not improve the conductibility. The number of auricular beats diminished a little, 61 beats, instead of 66, as in the former tracing.

Record no. 51-B.

An hour after the atropine injection the auricular rate has returned to 66 per minute without changing the auriculo-ventricular dissociation.

Observation no. 53.

Total block. Stokes' syndrome.

M. R. L., white, female, 38 years old resident at Curvello.

The patient states that she has had undefined attacks of fever for about five years. About a year ago she had fever again, with edema. Traces of hypoovarism, deficient menstruation. Very marked bronze coloring. Thyroid slightly hypertrophied Convulsive crises, which come on at irregular intervals of a week or more. During the crises the convulsions sometimes recur every five or ten minutes. Painful sensations. A feeling of pain and prickling over her heart. Pulse slow, 33 beats, accompanied by cardiac beats. Sometimes extrasystoles. The analysis of the tracing shows that it is evidently a case of total block.

Record no. 52.

Radial pulse ample, slow, beating at unequal intervals and with unequal amplitude A perfect analysis of tracing cannot be made as the marking of the time was defective. Heart tracing ample, the auricular waves with exceptional rises; it is only by their location in different points with relation to the rises of the ventricular systoles that the diagnosis of cardiac block can be made. The jugular pulse confirms this diagnosis. The *a a* waves are very frequently repeated, and rhythmically, not in relation to the *c c* waves. For each group of 10 *c c* waves there are more or less 26 *a a* waves. The block is total.

Observation no. 54.

Total block. Stokes-Adams' syndrome.

G. S., white, male, 50 years old, married, resident of a place near Lassance.

First examined April 9, 1910. Previous history obscure; he only mentions vague attacks of fever. For about ten years he has had giddiness and fainting fits which last from fifteen to twenty minutes. Hypertrophy of the lateral lobes of thyroid. Pulse slow, 37 beats; number of heart beats the same. On auscultation there seems to be a murmur added to the second sound, probably auricular.

April 13, 1910.

Pulse beats equal to heart beats; that is 29. General condition middling. Dyspnea on exertion, after walking quickly, or heavy work. When walking at ordinary pace the patient can however do four leagues and more without much fatigue. No dyspnea when lying down and sleeps well in horizontal position. No edema and no more giddiness. Heart enlarged, apex beat in fifth intercostal space at the level of mammillary line. Transverse diameter 14 cm. First sound lengthened and muffled. Systolic murmur at apex with small area of propagation. Second sound reduplicated with pulmonary accentuation. During the diastole a

muffled isolated tone is heard corresponding to auricular systole. Pulse rate: standing 25; lying down 24.

Katzenstein { before — 24 ps. Tmx. 105. during — 25 ps. Tmx. 100 after — 25 ps.

Liver and spleen not enlarged.

Examination August 17, 1913.

General condition middling. Subjective symptoms almost nil. No edema. Heart enlarged. Transverse diameter: 15,5. Pulse rate 29, not changing in different positions. Tmx.=130. Sounds muffled. Auricular tone with non-transmitted auricular systoles, distinctly audible during the ventricular diastole. Beats of neck veins very visible. Liver slightly augmented, not painful on pressure. The patient died suddenly in 1916 whilst at work.

Records nos. 53, 53-A and 53-B.

I) The radial and cardiac records similar; beats slow and rhythmic, rate 30 per minute.

In the venous record there are more frequent auricular waves, one ventricular wave to every three auricular waves, of which two are blocked; there Is regular block in the rhythm of 3:1. Is it block or simply coincidence that the auricular is three times more accelerated than the ventricular one? It is impossible to decide this point by the record of the tracing.

II) and III). These records taken at intervals of one or two years from the preceding clearly show the complete block. The ventricles beat at their own idioventricular rhythm. In record II the beats are not rhythmic, there beiug slight variations between one cycle and the other.

Observation no. 55.

Total block.

J. C. B., white, male, 30 years old, resident at Paraopebeba.

Previous history obscure. The patient complains of dyspnea on exertion and giddiness. No vertigo. Lateral lobes of thyroid hypertrophied. Liver enlarged. Pulse slow and regular, accompanying the heart beats. Rare extrasystoles. Pulse rate 34 beats. The simple inspection of neck veins already shows distinct signs of alterations of conductibility.

Examined August 24, 1912.

Generel condition middling, with relative compensation. Good appetite, normal digestion. No dyspnea either at night or when lying down. Dyspnea on exertion. No giddiness or seeming epileptic fits. No edema. The patient states that his feet and hands go to sleep and feel cold. Heart enlarged; apex beat 11.5 cm. from the midsternal line. Right margin 4 cm. from the same. Sounds muffled. In the ventricular diastoles is heard a short tone of isolated contraction of the auricles, without fixed relation to the ventricular systoles. 38-40 beats to the minute. Tmx.=110. Liver en larged, hard, painful on pressure.

Records nos. 54 and 54-A.

February 12, 1911.

Cardiogram and sphygmogram of slow, regular rhythm, exactly corresponding to one another. In the diastolic phase on the cardiogram are seen auricular waves which are not in relation to the ventricular systole. These waves are also marked in the catacrotic phase of the pulse. It is these characteristics that allowed us to affirm that there is a total block which is confirmed by the analysis of the venous record. The *a* waves more frequent than the ventricular waves which do not depend on them. The ventricles beat according to their own idioventricular rhythm. Record 54 a is not to be distinguished from the preceding; it shows the persistence of the block at an examination made a year and a half later.

Observation no. 56.

Auricular tachysystole (auricular flutter)

F. N., male, 25 years old, resident at Lassance.

May 15, 1911.

Sign of cardiac insufficiency. Palpitation. Rate standing 32, lying down 64. Arrhythmic pulse, with numerous lapses. Liver enlarged. Peripheral glands enlarged. Considerable hypertrophy of thyroid.

June 22, 1911.

General condition without perceptible change. Cardiac beats more regular, 44 when standing, 40 lying down. Tmx.=125.

In July, 1912, he came back to consult us, complaining of strong dyspnea and palpitations.

Heart greatly enlarged, apex beat in fifth space outside the nipple. Tachycardia with arrhythmic pulse, number of pulsations varying between 120 and 130. Cardiac excitability. A rapid examination was made, and we decided to move the patient to the Hospital. On the following day we heard that he died suddenly at his own house in syncope.

Records nos. 55-A and 55-B.

I) The cardiac beats and those of the radial pulse at slow rate, 55 beats, very arrhythmic, the diastolic pause varying from one cycle to the other, although within narrow limits. In the radial record the *a* waves accelerated, 230 a minute, not all accompanied by ventricular systole. A great number blocked very irregularly, sometimes in 3:1, sometimes 4:1 rhythm. The change in the rhythm of the block explains the irregular pulse.

II) Taken 1 month after the former. Pulse slower, 42 beats; some beats of extrasystolic aspect. The duration of the diastolic phase is very variable. The auricles beat with the same frequency, 230 to the minute. The block is more intense, the rhythm being 4:1 or even 7:1. The most frequent is 4:1.

III) About a month later another record was made; it is not worthy of special mention. The frequency of the auricles is increased to 250. This is a case of auricular tachystole with block of varying rhythm.

Observation no. 57.

Auricular tachysystole (auricular flutter) Cardiac insufficiency.

M. A., mulatto, female, 45 years old married, resident at Curralinho.

Examined Sept. 16, 1912.

Until about two months ago she had only waves of heat with abundant perspiration. Five months ago menstruation, which until then was quite regular, ceased. For the last two months this patient has had nervous excitement and sleeplessness. Dyspnea at night and when lying down so that she can only sleep propped up; sleep is agitated and broken by starts. Dyspnea on exertion. General edema more marked and in lower extremities and lower part of body. Constant dyspnea and cough.

Heart greatly enlarged. Apex beat 15 cm. from the midsternal line on a level with the axillary line and much lowered. Right margin 5 cm. from the midsternal line. Systolic murmur at apex, audible at the back. First sound audible in the tricuspid area. Second sound reduplicated. No murmur in basal area. Pulse entirely arrhythmic. Tmx.=115. Liver much enlarged, painful on pressure. Thyroid enlarged, with cystic goiter.

April 18, 1912.

Improvement of all the symptoms. Edema nearly disappeared. Dyspnea improved, so that the patient lies down. The cough has almost disappeared. Little change in the physical state of heart. Complete arrhythmia. Incipient bigeminism. 64 radial pulsations. Tmx.=120.

September 22, 1912.

After she was discharged and getting ready to leave the Hospital, she died suddenly. The post mortem showed that death was due to a rupture of the anterior wall of the right ventricle with intrapericardial hemorrhage. The histopathologic examination was made by Professor Crowell.

Records no. 56 and 56-A.

I) The heart and pulse records show marked ventricular arrhythmia, so that the dominant rhythm could not be fixed. The beats are frequent and completely irregular; in the jugular record are seen auricular waves in rhythmic succession and with great frequency: 290 to the minute. The ventricle does not answer to all excitations, many being blocked in a variable way from one to another cycle. Some beats apparently extrasystolic though it is impossible to say if they really are.

II) Taken three days after the latter; the patient had taken digitol. The number of auricular beats diminished a little, from 290 to 260. The auricular waves well marked; in the venous pulse they are irregularly blocked and the digitol has intensified the block; in some points there are 7 auricular beats to 1 ventricular one. The ventricles beat more slowly on account of the more intense block, but still very irregularly.

Observation no. 58.

Auricular tachycardia with transition to fibrillation. Cardiac insufficiency.

A. M., mulatto, female, 35 years old, living in Pirapóra.

Signs of cardiac insufficiency. Heart enlarged; 62 beats with extrasystoles and alterations of conductibility. Tmx.=100. Liver enlarged. Large goiter. Strong bronze coloring.

Examined April 19, 1912.

She complains of general uneasiness with great sadness. Dyspnea on exertion which has increased gradually to such a point that it appears even when resting; it is accompanied by a cough. Lately edema appeared. She has vertigo sometimes with falls. Heart greatly enlarged, the base line measuring 16 cm. The heart beats shake the thoracic wall; and the rate is sometimes 107. Many systoles are not perceptible in the pulse, where 56 beats are to be counted. Systolic murmur at apex, propagating itself to axilla. Tmx.=120. Tmn.=95. Liver much enlarged. Spleen enlarged and hardened. Thyroid with some hard nodules. Congestion of pulmonary bases especially the left. The condition varies; the patient is sometimes better, sometimes worse.

July 23, 1913.

General condition worse. Stitch in left side. Intense dyspnea. Cyanosis. Bloody sputum. Slight edema of lower extremities. Cardiac beats very irregular, now slow, now fast, sometimes very frequent, with trembling that cannot be counted. Pulse varying, on an average 56 beats. Heart much enlarged. Apex seventh space, 14 cm. from the midsternal line. Right margin 2 cm. from middle line. Liver enlarged. Signs of pulmonary engorgement at the right base.

July 28, 1912.

Pleurisy with effusion on the right. Bloody sputum. Cardiac bigeminism (digitalic) 78 heart beats; pulse 39. No perceptible change in the size of the heart. No murmurs. Sleepiness. Vomits. Cough with bloody sputum. Pain at the right side of thorax. Cyanosis. Slight edema of lower limbs. Pleural effusion increased. Bigeminism continues. 68 cardiac beats; radial pulse 39. The pleural fluid was extracted, and was serohemorrhagic. Patient got alternatively better and worse, and died on August 22, 1912 in syncope.

Records nos. 57, 57-A, 57-B and 57-C.

I) Examination of the three records shows first the great irregularity of the radial pulse and of the cardiac beats which succeed each other arrhythmically, at a rate of more or less 93 beats. The auricles beat perceptibly twice as often as the ventricles, 170; auricular *a* waves are seen in the jugular pulse. The irregularity of the pulse comes from the block of the auricular waves, in varying numbers, from one cycle to another, and perhaps from extrasystoles.

II) This record was made about a year after the other and shows the radial pulse with the appearance of a completely ar-

rhythmic pulse. In fact there is no method whatever in the order of beats which succeed each other in a completely arrhythmic and irregular way; the cycles vary in duration from one to the other and the amplitude is not in direct proportion to the durration of the preceding pause. In the jugular pulse are seen little waves which recur with great frequency, about 500 a min, ute. These represent auricular contractions-almost fibrillation, which appear in the following record.

III) Was made about one month after the last one. In the jugular pulse it is seen that the ventricular waves appear as acute rises in some points and that the signs of movement of the auricles are marked by small undulations. The pulse is completely arrhythmic.

IV) Two days afterwards, under the influence of digitol, the venous pulse has the appearance of a ventricular venous pulse; there are series of bigeminal pulsations, one of which is seen in the record.

Observation no. 60.

Auricular fibrillation. Cardiac insufficiency.

E. J. M., mulatto, 50 years old, married, laborer, resident at Lassance.

Examined December 8, 1912. Previous history, malaria. For about five months he has been feeling ill with fatigue on exertion, which he had never felt before. No dyspnea on lying down or at night, sleeps well. He has had slight and transitory edema. His legs feel heavy. Giddiness at times very marked. Attacks of palpitation which come several times a day; strong and rapid heart-beats, coming on without apparent cause and causing agony. Sometimes the beats are strong and slow, "measured"; his heart seems to be "pushing". At present edema of legs and abdomen. Heart much enlarged; apex in the seventh space on a level with the midaxillary line, 16 cm. from the midsternal line. Inside apex there is systolic retraction of the fifth, sixth and seventh spaces. Right margin 4 cm. from the midsternal line. First sound lengthened, dull, without murmur. Second sound reduplicated. Beats arrhythmic and slow. Precordial shock strong, shaking the whole precordium.

Katzenstein { before—51 Tmx. 125.
during—52 Tmx.
after—48

Liver enlarged and painful on pressure. Spleen same. Thyroid much enlarged.

Dec. 9, 1911.

Palpitation during the night and early in the morning; 47-48 beats. Complete arrhythmia. Tmx.=125. Atropine did not perceptibly modify the pulse.

December 10, 1912.

Slight improvement.

December 12, 1912.

More marked improvement; was discharged. He died months later in asystole.

Record no. 59.

Pulse absolutely irregular. The beats succeed each other in varying spaces, so that it cannot be foreseen where any given beat will fall. There is also no direct and constant relation between the preceding pause and the amplitude of the beat. At first sight it seems to be a bi—and trigeminal pulse, but there are many variations. In some points there are pauses which seem to be compensating pauses and do not appear in other points. The jugular pulse has the characteristic appearance of a ventricular venous pulse. The only really distinct waves are *c* and *v*. The *a* wave does not appear on the record. Rate of beats slow. At some points of the long diastolic phases (before and after the beat) are seen small undulations, which might he considered as the auricular fibrillations which exist in these cases. The same aspect of fibrillation is seen in the heart record. It is a case of complete arrhythmia, with ventricular venous pulse and auricular fibrillation. The records I, II, and III show slow rate with complete arrhythmia and ventricular

venous pulse, which I compared with II and III shows that atropine does not appear to have modified the arrhythmia.

Observation no. 61.

Complete arrhythmia. Cardiac insufficiency. Spasm of esophagus.

P. N. A., black, female, 41 years old, single, living in Vargem da Palma.

Examined August 24, 1913.

General slight edema. Turgidity of neck veins. Gastric disturbances. Lack of appetite. Spasm of esophagus, great difficulty in swallowing solid food so that she is obliged to drink water after each mouthful. Dyspnea on exertion and when lying down.

Heart much enlarged, apex beat beyond the anterior mammillary line. Right margin 5 cm. outside the midsternal line. First sound accompanied by systolic murmur, audible at the back. Number of beats lying down 66; seated 72; standing 82. It is difficult to count as there is complete arrhythmia. Tmx.=135. Liver much enlarged. Spleen not enlarged. Thyroid with large goiter.

August 28, 1912.

Improvement of all the symptoms by treatment; no change in cardiac area.

Record no. 60.

The radial, cardiac and jugular tracings are similar; the latter has the aspect of ventricular venous pulse. The waves are bi- and trigeminal but the intervals between them are most irregular. It is a tracing of complete arrhythmia of auricular flutter; the *a* waves do not appear on the jugular tracing.

Observation no. 62.

A. S., male, white, 33 years old, widower, laborer, resident in the neighborhood of Lassance.

Examined April 13, 1913.

Very short but robust. Marked paleness of skin with special coloring. Mucous membranes rather discolored. Slight not constant edema of face. Previous history; nothing worth mentioning. Had grippe during the great epidemic. For about three years he has had a feeling of fatigue on the slightest exertion; he gets tired after quick walking or climbing up hills, or even when at his usual work. Sometimes has palpitation and feels as if his heart were stopping. He is subject to giddiness, which comes on after exertion or even without any perceptible cause. Heart not enlarged. First sound slightly muffled; second not altered; there is mesosystolic murmur in the pulmonary area. 76 beats, with frequent extrasystoles, which appear either isolated or in long bigeminal series. Arteries not hardened. Thyroid enlarged, with cystic lobules. Examination of other organs negative.

In her house were found numerous infected specimens of Triatoma.

Several electrocardiagraphic records were taken of this patient. We give n. 1 and 2 Complement fixation reaction positive (with heart of a dog infected by *Tryp. Cruzi* as antigen).

Record no. 61.

Was made with derivation 1 (right arm—left arm). The time marked is 1/25 of a second. The derivation of the galvanometer is 2 cent. to 0.001 volts. The left side of the record shows a succession of rhythmic regular contractions, in which note the deviations P. Q. R. S. and T. The PP. waves have nothing interesting about them. The space PQ is within the normal limits, less than one fifth of a second. S phase does not appear. T is inverted in all the cycles. At the right side of record are seen 4 extrasystolic beats in bigeminal series. The extrasystoles are of ventricular origin and of the type which springs from the area situated in the right ventricle. The variation of the auricular systole appears in the diphasic variation of extrasystole in normal time.

Record 2 of the same patient. Derivation III (left arm-left leg). Time 1/50 of a se

cond. The tracing shows a succession of extrasystolic beats recurring alternatively with normal cycle. The derivation *R* is bifid. *S* appears in this deviation and *T* leaves ofbeing inverted. The extrasystoles are of ventricular origin, probably from the righe ventricle. The deviations *P* keep their rhythmt marked in the diphasic variation of the extrasystoles.

Observation no. 63.

F. Mor., mulatto, male, 30 years old, married, laborer, resident in the neighborhood of Lassance.

Examined April 13, 1921.

Is of medium height, well-built and of robust appearance. He did not come to consult a doctor and was only examined as he had a daughter under our care, who had an acute form of trypanosomiasis, with numerous parasites in the peripheral blood. He lives in a house infested with infected triatomes. Previous history: nothing worthy of notice. There are no subjective symptoms except rather easily brought on fatigue, and sometimes lapse of the pulse, though he did not pay much attention to this. The objective examination reveals a slight increase of the cardiac area, and numerous extrasystoles, without other perceptible alterations of circulatory system. Thyroid enlarged, with hard cysts of different sizes not being bigger than a walnut. The examination of other systems proved negative.

Complement fixation reaction positive (with heart of a dog infected by *Tryp. Cruzi* as antigen).

Several electrocardiagraphic tracings were taken; we give Ns. 3, 4, 5 and 5a.

Electrogram no. 3 was made with derivation I. T=1/50"; 1 cm.=0.001 volt. Two extrasystoles are seen on the right side of record, which interrupt the regular succession of the heart beats. In the beats of the normal cycles are marked waves *P*, *Q*, *R*, and *T*. The space *P Q* is normal. *T* is inverted in all the cycles; *S* does not show. The waves *P* succeed each other regulary; they are seen in the extrasystolic variation where they are marked. The extrasystoles are ventricular and come from the right ventricle. Record no. 4 came from patient taken in derivation II (right arm—left leg). Two extrasystoles are seen on the left of the record, both probably originating in the right ventricle. In the beats of the normal cycles it may be seen that *P* is frankly bifid. In the cycle which follows the second extrasystole *P* is inverted, without there being premature auricular contraction. *T* is inverted in all the cycles. It is clearly more marked in the cycles which follow the extrasystolic beats which is a common fact. *S* is deeper in this derivation, and that corresponds to the predominance of V E. Records 5 and 5-A were taken at the same time as the former ones but in D III. P is much more elevated; it is still bifid. The PP waves are arrhythmic. *S* is less deep. *T* still appears inverted. In both the records are seen extrasystoles of ventricular origin. The last of both the records comes from the left ventricle, the others come from the right vntricle.

On a rare type of necrosis of the liver

by

Dr. C. Magarinos Torres.

(With plate 32).

Following Dr. B. C / CROWELL's advice and instructions, I made a study of some anatomical lesions of the liver found during an autopsy which are comparatively rare.

Necrosis of the liver may be central or focal. In focal necrosis, there are small necrotic areas in the hepatic lobules, which are not in direct relation with the central vein; this type is found in acute infectious diseases such as pneumonia, yellow fever, eclampsia, scarlet fever and diphtheria. These lesions are sometimes of infectious and sometimes of toxic origin.

In central necrosis, the lesions surround the central vein of the lobule and are due to toxic conditions. This kind of necrosis is often observed in certain infectious diseases, and also in some other cases; it is found, for instance, in acute yellow atrophy of the liver and also in chloroform poisoning. Central necrosis with hemorrhage is found in some cases of chronic passive congestion. In a recent paper on chronic passive congestion, LAMBERT and ALLISON (1) indicate the following five types of lesions:

A) dilatation of the capillaries with atrophy of the central cells of the lobules:

B) central degeneration with or without dilatation of the capillaries:

C) marked fatty infiltration in the cells around the hepatic vein, with congestion of the middle zone:

D) central necrosis with hemorrhage:

E) Cirrhosis of cardiac origin.

I shall have to refer to some of these types of lesions while describing the present case, though strictly speaking, these types were not found in our case.

It is not difficult to observe our type of necrotic lesion in experimental conditions and it is often found in other organs at post-mortem examinations; it has no apparent connection with the limits of the lobules, and is associated with a relatively slight inflammatory reaction.

Microscopic preparations revealed thrombosis of some capillaries of the liver caused by long, thick, rectilinear or slightly curved, Gram-positive bacilli without spores or capsules (*Bacterium coli ?*). These capillaries were found more or less in the centre of the necrotic areas, but some were found in the liver tissue not necrosed.

The liver is enlarged and macroscopically the appearance of the lesion is quite peculiar. (Plate 32, Fig. 2).

The lesions may be partly explained by the bacterial thrombosis of the capillaries, if one supposes also the existence of a toxin

(1)—LAMBERT, R. A. and ALLISON, B. R.—Types of Lesion in Chronic Passive Congestion of the Liver (Illustrated).
Bull. of the John Hopkins Hosp. 1916. XXVII. 350.

chronic passive congestion due to compression of the vena porta by a much enlarged lymphatic gland of the hilus of the liver must also be taken into account.

The process was evidently acute and recent, the subject being a young male, 22 years old, whose clinical history is unknown.

The autopsy was made 10 hours after death.

From the protocol we extracted the liver description and the anatomic diagnosis.

Liver – Liver enlarged; left edge in contact with the left abdominal wall covering the stomach, spleen and left kidney.

Weight 3.200 grs.

A lymphatic gland enlarged to about the size of a hen's egg envelops the common bile duct like a short sleeve; it is yellowish and soft. On section the pulp is found to be yellowish and gelatinous.

Bile ducts perfectly permeable, not compressed by the above-mentioned gland.

Liver surface reddish brown, capsule smooth, transparent, shining. On the antero-superior surface some white lines ramified like branches, which form a net with large meshes. In certain parts of the surface, small yellowish confluent spots with clear edges can be seen through the capsule; their diameter is about 3 or 4 mm.

General color of surface of section dark brownish-red. Lobular outlines indistinct; connective tissue not increased.

There are small confluent yelllowish areas of different sizes, the largest 3 or 4 mm. in diameter, the smallest hardly visible distributed over the whole of the liver, but especially in certain regions a round the capsule. Hepatic tissue around these areas, and all over the liver, dark brownish red in color.

After fixing in 10% formol, the specimens changed from the general brownish red color, when fresh, to a more or less marked brown. After the piece was fixed the small foci of necrosis became more distinct, looking like small opaque spots of a light yellowish-green color, the larger ones measuring 2-3 mm. in diameter, neither prominent nor depressed. (Plate 32, Fig. 2). The hepatic tissue forms a slender ring of more accentuated brown color (congestion) than the rest of the tissue.

In some places, there are 2 or 3 small foci almost touching each other, the zone of hepatic tissue that separates them not being more than 2 or 3 mm. wide; about 3 or 4 cms. from such a group one finds other similar groups. The distribution of the lesions is thus irregular; in certain regions, chiefly around the capsule, the kind of group just described; in other regions mostly in central part of the organ, the foci are fewer, and appear as isolated spots in the midst of the dark brownish mass of the liver tissue, (dark brownish-red when fresh).

Anatomic diagnosis:

Icterus.

Hyperplasia, hyperaemia et necrosis hepatis.

Hyperplasia nodoram lymphaticorum hepaticarum et lumbarum.

Nephritis parenchymatosa chronica.

Hypertrophia et dilatatio ventriculi sinistri.

Oedema pulmonum.

Pleuritis chronica adhaesiva.

Leptomeningitis chronica, (syphilis ?).

Hypoplasia lienis.

Microscopic description

Fragments of the liver, in which the lesions were very marked, were removed at the time, fixed in ZENKER-FORMOL (ZENKER'S LIQUID without acetic acid).

The paraffin sections were stained by hematoxylin-eosin; other fragments were fixed in 10% formol and stained by Scharlach R-hematoxylin.

Some of the lesions were distributed over the whole liver, others were focal lesions.

A) Focal lesions

I will describe two of the most typical of these lesions, of which there are many variations, some of them representing more,

and others less advanced stages of the same process.

Ist. Aspect.

These lesions have distinct outlines. (Plate 32, Fig. 1). They are round shaped and coincide with the hepatic lobules, in the centre of which is the efferent vein.

Often two or three of these lesions merge into one another, so that the outline of one or more of the contiguous spaces disappears.

They look then like a badly made 8, or a roughly drawn bunch of grapes. In each zone may be distinguished a central spot and marginal ones.

a) Central part

The liver cells, blood corpuscles, capillary endothelium and migratory cells become necrotic.

The trabecules of REMAK which can be recognised, are decreased in number, the cells which form them are deeply stained by eosin, and become very distinctly outlined, their granular protoplasm contains vacuoles, the nucleus is hardly seen or not at all (karyolysis).

It is easier to identify the cells by their mutual relation than by their structure (Plate 32, Fig. 1). The capillary walls are unaltered and show a clear outline.

Between the capillary walls clearly outlined and the trabecules there is a clear space where are found a few migratory cells and spheric masses which eosin stains red, and which are cellular detritus.

The liver sinusoids are much enlarged and very unequally. The lumen is occupied by spherical vacuolated masses which do not take eosin or hematoxylin stains, some of them are blood and others migratory cells.

In some of the areas of necrosis, one or more capillaries are completely obstructed by bacilli. These thrombotic capillaries are found more or less in the centre of the lesion.

The bacilli are Gram-positive, long, thick straight or slightly curved. No capsule so spores were noticed. Unfortunately, no cultures were made at the time of the autopsy; it is therefore impossible to identify them.

They are very much like *Bacterium-coli* in appearance and staining properties. I also found capillaries outside the area of necrosis in more or less well preserved hepatic tissue, containing masses of bacteria with the same characteristics.

b) Margins

The lesions just described are clearly limited on the outside by a narrow zone of tissue where the capillaries are very much dilated and full of blood cells which stain well with eosin; round them are many migratory cells and leucocytes with polymorphous nuclei (Plate 32, Fig. 1). This narrow zone serves as a dividing line or uninterrupted frame which separates the necrotic degenerate areas from the neighbouring hepatic tissues. The focal lesions just described are often if not always surrounded by the following ones.

2nd Aspect

When observed with a low power, some of the sections of this liver show zones where the sinusoids are very much dilated and full of blood corpuscles and liver cells in which are seen signs of regressive changes. Some of these zones are small and round. Most of them however form narrow bands which are several times as long as the microscopic field.

The relations between these lesions and the hepatic lobules are not clear. The only evident fact is that they are found far from the portal spaces, from which they are separated by a region in which the liver tissue has retained its structure comparatively well. This brusque contrast is one of the best characteristics of the lesions.

At the level of the above-mentioned zones, the protoplasm of the hepatic cells stains deeply with eosin; it is granular and contains 2 or 3 larger vacuoles as well as many small ones. The outline of the cells ris very distinct. The nucleus of the cell oc-

cupies anexcentric position in the protoplasm; it is oval and not very distinct; the details of its inner structure are not visible as it stains rather diffusely with hematoxylin (karyolysis).

There are a few other hepatic cells, the nuclei of which are no longer visible; the protoplasm of these cells is vacuolated and stains deeply with eosin; in the marginal zone there are large granules some of which are close together, whereas others are far apart; the cellular outline is interrupted in that point.

In other cells the protoplasmic disaggregation is more marked, and there are spots where the hepatic cells are only round masses which take a uniform reddish-pink color, when stained with eosin; they are small and are found in groups of three or four different sizes.

The arrangement of the cells in trabecules of REMAK is completely blurred by the necrosis of the liver-cells.

In the focal lesions just described, the hepatic cells are isolated, or are remnants of the trabecules of REMAK composed of 3,4 or at most 5 contiguous cells, all of which have the above-described appearance.

The liver sinusoids are dilated and filled with red blood corpuscles and migratory cells.

The most characteristic feature is certainly the presence of a great number of migratory cells which surround and limit the capillaries. These cells are very active phagocytes, as can be seen by the large quantity of material accumulated inside their protoplasm.

The lesions above described have some affinity to the lesions found in chronic passive congestion. It is, however, impossible to include them in any of the five types described by LAMBERT and ALLISON.

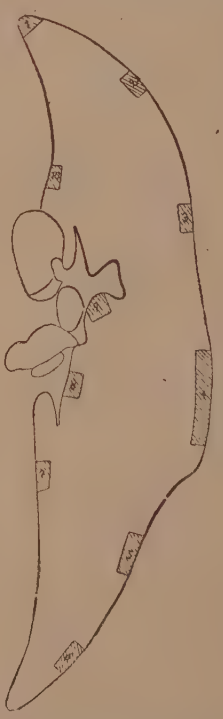
I noticed, on the other hand, that this type is always present in sections where the first aspect is found, or in sections which include bacterial thrombosis of the capillaries.

The lesions of chronic passive congestion found all over the liver make the achracteristics of this type of lesion very undecided indeed.

B) Diffuse lesions.

Some of the types of chronic passive congestion described by LAMBERT and ALLISON were found all over the liver.

Pieces removed from the liver which is now in the Anatomical Museum of the Instituto Oswaldo Cruz, account for the distribution of the lesions (v. diagram). This specimen comprises a longitudinal section of the whole liver, passing more or less through the middle of the antero-superior surface.



Block 1: chronic passive congestion (central degeneration with or without dilatation of capillaries).

Block 2: Chronic passive congestion (dilatation of the capillaries with atrophy of the cells of the centre of the lobule).

Block 3: Acute diffuse hepatitis (lst and 2nd aspects). Chronic passive congestion (dilatation of the capillaries with atrophy of the central cells of the lobule).

Block 4: Chronic passive congestion (dilatation of the capillaries with atrophy of the central cells of the lobule and central degeneration, with or without dilatation of the capillaries).

Block 5: Thrombosis of a capillary by masses of bacteria (bacilli). Chronic passive congestion (dilatation of the capillaries with atrophy of the cells in the centre of the lobules and central degeneration, with or without dilatation of the capillaries).

Block 6: Thrombosis of a capillary by masses of bacteria (bacilli). Chronic passive congestion (dilatation of the capillaries with atrophy of the cells in the centre of the lobules).

Block 7: Acute diffuse hepatitis (2nd aspect). Chronic passive congestion (dilatation of the capillaries, with atrophy of the cells of the centre of the lobules and central degeneration, with or without dilatation of the capillaries).

Blocks 8 & 9: Chronic passive congestion.

Block I0: Acute diffuse hepatitis (lst. & 2 nd. aspects) and thrombosis of the capillaries by bacteria (bacilli). Chronic passive congestion.

We would here tender our most sincere thanks to Dr. B. C. CROWELL, under whose direction this work was carried out, for his patient instructions and kind advice,

Explanation to Plate 32.

Fig. 1 — Section through liver, haematoxylin-eosin stain.

Acute diffuse hepatitis (1rst aspect).
The areas coincide with the hepatic lobules; in the centre of the latter the efferent vein.
The trabecules of REMAK are reduced in number and constituted by necrosed cells; the clearly outlined lighter spaces between the cells represent dilated capillaries with necrotic migratory cells and blood corpuscles.
Round the focus of necrosis a narrow inflammatory zone.

Fig. 2. — Macroscopic appearance of lesion.

Circular or oval areas of a light yellowish-green, neither prominent nor depressed, round which the hepatic tissue constitutes a narrow ring a pronunced brownish tint.

Revision of the family CUCULLANIDAE, Barreto 1916 (1)

by

Dr. ANTONIO LUIZ DE B. BARRETO.

(With plate 33–46.).

Material.

The present paper contains the result of helminthological research work made in fishes of our coast. However, it only embraces those representatives of the genus *Cucullanus*, which I was the first to describe. The numerous fishes examined came not only from the Bay of Rio de Janeiro, but also from the Ilha Grande, an island to which I made an excursion at the end of 1916.

Cucullanidae B. BARRETO. In the year 1916, I added the new family *Cucullanidae* to the already existing families of *Nematodes*.

Already in 1915, RAILLIET & HENRY, when studying the genus *Cucullanus* MUELLER, 1777, noticed the great confusion that reigned amongst the different authors from DUJARDIN onwards, about the representative genus *Cucullanus* and *Dacnitis*, DUJ., 1845. They came to the conclusion hat the name *Cucullanus* MUELLER, 1777 ought to be given to the species then included in the genus *Dacnitis* DUJ., 1845, of which the type is *Dacnitis esuriens*, DUJ., 1845. This species was identified by SCHNEIDER with *Cucullanus foveolatus*, RUD., 1809 and *Cucullanus cirratus*, MUELLER, 1777 by RAILLIET and HENRY.

The genus of MUELLER is however completely different from that to which DUJARDIN and after him all the other authors gave the name *Cucullanus*, with *Cucullanus elegans* ZEDER, 1800 as type species. It was time to change the name of this last for which RAILLIET & HENRY proposed the name of *Cucullanus*.

I am of the same opinion as RAILLIET & HENRY who think that the *Dacnitis*

(1) In 1913, RAILLIET & HENRY changed the sub-family *Heterakinae* into a family composed of five genera, amongst which is *Dacnitis*.

DUJ., 1845 cannot be considered aught but a synonym of *Cucullanus* MUELLER, 1777 (type: *Cucullanus cirratus* MUELL, 1777) and also that the genus *Cucullanus* DUJ., 1845 ought to be named *Cucullanus* RAILLIET & HENRY, 1915 type-species *Cucullanus lacustris* ZOEGA 1775=*Cucullanus elegans* ZEDER, 1800.

In the same year, TRAVASSOS showed the necessity of excluding the genus *Dacnitis* DUJ., from this family which should rather be called *Cucullanidae* than *Dacnitidae*, as LANE thinks on account of the following characteristics.

Cucullanidae nov. fam.

(nec DIESING, 1861. Camallanidae, RAILLIET & HENRY, 1915)

Polymyarians. Mouth with two lips. Oesophagus with dilated anterior extremity forming a sub-oral capsule. Bulb wanting.

Male: Sucker without chitinous rim; two spicules with accessory piece.

Female: Vulva near middle of body. Uterus duplex. Eggs hatched out.

This family includes only one genus: *Cucullanus* MUELL., 1777. We do not accept LANE's genera *Serradacnitis* and *Bulbodacnitis*, as the presence of the saw-like teeth on the rim of the oral capsule characteristic of the first-named genus, exists in all the representatives of this group. The cephalic dilatation justifying the name of *Bulbodacnitis* does not seem to be a generic character, as it is found in one species.

Genus CUCULLANUS (MUELLER, 1777) RAILLIET & HENRY, 1915.

(For list of synonyms see portuguese text p. 70).

Diagnosis:

Cucullanidae: Cephalic extremity generally turned towards dorsal surface. Mouth ellipsoid with large dorso-ventral axis, limited by two lips with saw-like chitinous apparatus and three papillae above them. Oesophagus rectilinear, anterior part dilated in sub-oral capsule, posterior half club-shaped; bulb absent. No lateral membranes.

Male: Sucker, small, spindle-shaped, without horny rim, slightly muscular. Spicules two, equal as a rule, not exceeding the posterior limit of sucker; accessory piece. Caudal alae rudimentary, sometimes absent. Caudal papillae arranged in two longitudinal rows, never more than 11 pairs.

Female: Vulva very prominent, opening in posterior half of body. Ovijector turned towards cephalic extremity. Uterus dichotomous with diverging ramifications. Eggs ellipsoid with smooth and very thin shell. Embryo developed when eggs laid.

Habitat: Intestinal tube of fishes.

Type-species: CUCULLANUS CIRRATUS MUELLER, 1777.

The genus *Cucullanus* includes 22 species at the present date, two of which are Brazilian. Some of these species are not well defined, there being some doubt as to their identity. Not being in possession of all the papers and treatises on the subject, I cannot attempt to draw a conclusion concerning them. To facilitate the study for those who, later on, may be interested in these nematodes, I give a list of the species in the litterature which I was able to obtain and which should be consulted. (See portuguese texte p. 71).

Brazilian species of the genus CUCULLANUS:

1. *Cucullanus pulcherrimus* BARRETO, 1918.
2. *Cucullanus dodsworthi* n. sp.

CUCULLANUS PULCHERRIMUS BARRETO, 1918.

Pl. 44, Figs. 1 e 2.

Dimensions { Length: 13 mm.; width: 0,445 mm. measured at middle of body. Length: 15,9 mm.; width: 0,472 mm. at height of vulva.

Yellowish-white rectilinear nematode with strongy dilated globulous cephalic extremity and sharply tapering caudal end. Anterior part of body dorsally curved, both in male and female, in some more so than in others. Posterior part sometimes rectilinear, generally turned towards the ventral surface. Cuticle not very thick, transversally striated; the striations 0,0036 mm. from one another, crossed by two or three light longitudinal striations. Anterior extremity spheroid, when looked at sideways, voluminous, easily seen by the naked eye; adjacent part of body slighter. At the level of the cephalic extremity near the angle of the lips, the cuticle presents a very characteristic series of ornaments. Two small lateral papillae are found a little below the oesophagus about 1,10 mm. from head. No lateral alae. Nerve collar situated at junction of anterior quarter and posterior three-quarters of oesophagus, 0,650 mm. from anterior extremity.

No excretory pore visible. Mouth bivalved with two divisions resembling the two shells of a mollusk. Free rim of the valves, covered with a serrated sheat of chitin, stretched from one labial commissure to the other. Each lobe with three external papillae one dorsal, one median and one ventral. Lips joined at the commissure by a delicate longitudinally striated membrane. Diameter of cephalic extremity: 0,483 mm. Width of lobes: 0,232 mm.

Initial part of oesophagus strongly dilated like an amphora, middle part slightly sinuous, posterior rectilinear and club-shaped. At the level of the dilatation which forms a kind of sub-oral capsule, the walls of the oesaphagus are very muscular and there is a lumen with a thick layer of chitin. At the bottom of the amphora-like dilatation, about 0,280 mm. from the head, a triangular chitinous prominence on each side of internal wall of oesophagus which I consider to be teeth. Beyond the sub-oral capsule the middle part of the oesophagus is somewhat sinuous and narrower.

Nerve collar at level of this segment. Posterior part of oesophagus rectilinear and club-shaped, opening directly into intestine by means of a special valvular apparatus.

Walls of oesophagus consist of three layers, outer one thick and abundantly supplied with transversal muscles, middle one narrow, separated from the former by a longitudinal, very refringent band of uniform aspect, with two lighter longitudinal lines; internal layer thinner, finely granulated, thickly covered with chitin, which completely closes the cavity. Length of sub-oral capsule: 0,318 mm.; width: (in middle) 0,232 mm. Oesophagus: Length: 590 mm.; greatest width: 0,251 mm. Intestine funnelshaped in initial part, covering posterior part of oesophagus; generally rectilinear and ending in a small rectum, 0,186 mm. in length, separated by a sphincter of transversal muscular fibres.

Male: Posterior extremity, slightly ventrally curved, suddenly tapering from anogenital ridge, funnel-shaped, ending in a sharp pointed chitinous formation, 0,026 mm. in length. Sucker small, ellipsoid, muscular, without chitinous ring, length: 0,279 mm.; rim of sucker 1,255 mm. from caudal extremity. Caudal expansions quite insignificant. Ten pairs of papillae, arranged in two longitudinal series, in the following manner:

Three pre-anal, ventral; two large, one above the sucker, another below, and a lesser one between sucker and anus nearer the latter.

Four ad-anal, of which three ventral arranged in a series, the first less than the two latter ones, and a small lateral one between the second and third ventral.

Three post-anal, small, equal, of which two ventral near the caudal extremity, and one lateral a little above the first ventral one.

Two small spicules equal in size, not attaining the lower limit of sucker, slightly chitinised, somewhat curved, with very dilated proximal and sharp-pointed distal extremity; length of spicules: 0,527 mm.; width: proximal extremity 0,076 mm.; in middle 0,022 mm. Gubernaculum, slightly chitinised, gently curved, 0,133 mm. long.

Anus opening in a slight ridge of tail, 0,372 mm. from posterior extremity.

Female: Tail straight, funnel-shaped with chitinous appendix, 0,030 mm. in length. Vulva situated behind the middle part of body, very prominent, cleft-like, with two large lips, one anterior the other posterior. Ovijector directed from the vulva towards the cephalic extremity, dilated in the posterior segment, followed by the vestibulum; approximate length: 0,465 mm. Uterus short, dichotomous, with diverging branches. Ovaries very large; ovarian loops reaching first part of intestine, but not exceeding anus.

Eggs ellipsoid with very thin shell, still in segmentation when laid; length: 0,083 mm.; width: 0,053 mm.

Development. Unknown.

Habitat. Intestine of *Caranx lugubris*, POEY.

Origin. Island of Trindade, Brazil.

Material. The specimens studied were taken from the helminthological collection of the Instituto OSWALDO CRUZ (No 1491). Five males and two females, preserved in glycerine.

CUCULLANUS DODSWORTHI n. sp. (1)

Plate 45, figs. 1 e 2. Plate 46, figs. 3 e 4.

Dimensions
- ♂ length: 9,54 mm.; width: 0,380 mm.
- ♀ length: 4,4 mm.; width; 0,445 mm.

Body white, filiform, rectilinear, tapering at extremities; posterior part curved like a hook, in males only. Moderately thick cuticle transversally striated; the striations are 0,0037 mm. from one another; longitudinal striations extremely fine and close together in optical cut, the cuticle seems to be formed of two layers, the external one almost hyaline, the internal one of more or less the same thickness, slightly granulated, separated from one another by an exceedingly refractory line; the thickness of cuticle: 0,0088 mm. Anterior extremity cylindro-conical, when seen dorso-ventrally apparently sub-quadrangular. Lateral alae wanting. At the height of the junction of the oesophagus with intestine, a pair of cephalic papillae which are very distinct when the nematode is seen from the side. Nerve collar at the junction of anterior fourth and posterior three-fourths of oesophagus, 0,372 mm. from cephalic extremity. Mouth formed by two thick equal lobes, each of which has three equal, external papillae, one dorsal, one ventral and one median; on internal surface each lip has two chitinous sheets of equal dimensions with reticular structure and dentate or serrate border; denticles like a short bayonet, the cutting sheets adhering by the posterior rim to the lobes' two-thirds of them free, and curved inwards in the oral cavity, so that, when seen in a dorso-ventral direction, they look like two lips forming the curves of a circle thus closing the buccal orifice; a fine membrane, part of the cuticle, unites the lobes.

Diameter of cephalic extremity; 0,270 mm.; width of lobes: 0,095 mm.

Oesophagus rectilinear, forming a large amphora-like dilatation in the buccal cavity, turned ventrally, thus forming a sub-oral capsule; in this part of oesophagus, the walls are very thick with strong transversal muscles; the inner wall is clothed with chitin; oesophagus rectilinear behind this dilatation, the posterior extremity club-shaped; walls of oesophagus muscular; gland less; proportion of oesophagus to body 1:7 in female, and 1:6 in male; length of oesophagus: 1,335 mm. Sub-oral dilatation, length: 0,279 mm.; width: 0,195 mm. Intestine dilated in initial portion which fills here more than two-thirds of the visceral cavity; the intestine before reaching the posterior extremity shows a sphincter which connects it with a small rectum; this is curved ventrally towards the anus which is generally on a slight ridge, especially accentuated in females.

Male: Accessory piece cylindroid, 0,114 mm. long; 0,015 mm. wide. Anus 0,186 mm. from posterior extremity of body.

(1) Species dedicated to my friend and colleague Dr. H. TOLEDO DODSWORTH JUNIOR.

Female. Tail, rectilinear, tapering, ending in chitinous spike. Vulva small, not prominent, opening in dent of cuticle, beyond the middle part of body, more or less at junction of posterior 1/3 and anterior 2/3. Ovijector, short rectilinear, forming acute angle with ventral surface, from vulva onwards, turned to cephalic segment muscular; lumen line with strong chitinous layer separated from horns by transversally lined sphincter, length: 0,325 mm. Uterus dichotomous, with diverging branches, each one opening into the bottom of ovijector by means of a short very muscular horn. Each uterine branch is provided with a long ovary; the uterine hooklets reach to the inner part of of the intestine and spread out near the rectum. Eggs ellipsoid, few in number. with very thin shell, not hatched when laid; length: 0,079 mm.; width: 0,045 mm. Anus 0,325 mm. from caudal extremity.

Development. Unknown.

Origin. Bahia de Guanabara, Rio de Janeiro, Brazil.

Material. Taken from the helminthological Collection of the Instituto OSWALDO CRUZ.

We tender our heartiest thanks to Dr. LAURO TRAVASSOS for his account of the helminthological studies made by him in the Island of Trindade, as well as for the excellent material he gave us.

We are also very much indebted to Drs. GOMES DE FARIA and MARQUES DA CUNHA for their help, and for the interest they took in the research work made during my stay on the Ilha Grande.

See portuguese text for { Bibliography p. 83. Explanation of figs. p. 87.

Contributions to the Knowledge of the Brazilian Helminthological Fauna:

XVI. Cruzia tentaculata (RUD., 1819)

by

DR. LAURO TRAVASSOS

(With plate 47–50).

The *Ascaris tentaculata* of RUDOLPHI is one of the three species included by SCHNEIDER in his genus *Oxysoma*.

RAILLIET and HENRY, when studying the *Oxyuridae* in 1916, found that the type of the genus *Oxysoma* did not correspond to *Fusaria brevicaudata* ZEDER, but rather to a new species for which they proposed the name *longespiculum*. The generic name of *Oxysoma*, being preoccupied, was then changed by the same authors to *Oxysomatium* (1913).

As we saw in 1917, the two remaining species of the genus of SCHNEIDER must become part of entirely different genera and families. The *Oxysoma leptura* has already been studied in detail by us (1918) and LANE (1914).

For *O. tentaculata* we proposed in 1917 a new genus and family, which we will now consider in more detail.

Cruzidae TRAVASSOS, 1917.

Characters: *Oxyuroidea* with imcompletely polymyarian musculature, rigid esophagus, with a large bulb and ample vestibule; intestine with a marked anterior diverticulum; median vulva; two nearly equal spicules and gubernaculum; female genital apparatus didelphic.

Habitat: Large intestine of marsupials.

Type genus: *Cruzia* TRAVASSOS, 1917.

This family has a great resemblance to the *Subulurinae* and also in some ways to the *Kathlanidae*, as there is a vestige of a bulb just above the true bulb.

The structure of the digestive apparatus is quite curious and separates it from any other group of the *Oxyuroidea*, since, aside from having an intestinal diverticulum directed to the front, it presents the anterior portion differentiated in a curious way, sho-

wing large papillary prominences which appear to have a function like that of the intestinal villosities of the vertebrates. The posterior extremity of the males also presents an interesting disposition since it is depressed and slightly excavated, appearing to have the function of a suction apparatus, besides having the cuticle corrugated and presenting obliquely disposed muscles as are noted in the *Kathlanidae*.

Up to the present this family has only one genus with only one species.

Genus *Cruzia*, TRAVASSOS, 1917.

Characters of the family:

Only species: *C. tentaculata* (RUD., 1819) TRAV. 1917.

Cruzia tentaculata (RUDOLPHI, 1819)

(Pl. Fig. 1—12.)

Syn: *Ascaris tentaculata* RUD. 1819 p. 168.

Ascaris tentaculata DUJ. 1845 p. 168.

« « DIESING, 1851 p. 147.

« « LEIDY, 1855 p. 51.

« « DIESING, 1860 p. 655.

Oxysoma « SCHNEIDER, 1866, p. 135 (pl. VII, fig. 13, p. XV, fig. 1).

Cruzia tentaculata. TRAV. 1917. Br. Med. Ann. 29, n. 12.

Length: ♂ ♀ 8 to 16 mm., the males being slightly smaller.

Breadth: ♂ ♀ 0,52 to 0,67 mm.

A helminth of white color, slightly motile, attenuated at the extremities, the greatest diameter being preequatorial; cuticle smooth, thick; mouth protected by three subtriangular lips; buccal capsule or vestibule narrow, trilateral, measuring 0,106 to 0,156 mm. in length; oesophagus cylindrical, with spherical bulb, measuring without the bulb 1 to 1,9 mm. in length 0,10 to 0,12 mm. in width; the bulb measures 0,31 to 0,48 mm. in diameter; intestine with anterior diverticulum about 0,9 to 1,2 mm. mm. in length; nerve ring 0,46 to 0,60 mm. from the anterior extremity; excretory pore 1 to 1,4 mm. from the extremity.

Female with the vulva in the mid portion of the body: ovijector claviform; ova 0,120 by 0,056 to 0,063 mm.; anus 0,8 to 1 mm. from the extremity; male with 9 pairs of papillae, 3 postanal approximate, 3 adanal and approximate, and 3 preanal, separated; spicules equal, 0,8 to 1,1 mm. in length; gubernaculum flat, 0,19 to 0,24 mm. in length; anus 0,21 to 0,29 mm.

Habitat: Large intestine of *Didelphis (D.) aurita*, WIED; *Didelphis (D.) virginiana* KERR (1); *Didelphis (Philander) philander* L.; *Didelphis (Philander) lanigera* DESM.; *Didelphis (Metachirus) opossum* SEBA; *Didelphis (Peramys) domestica* WAG.; *Didelphis (Mormosa) murina* L.; *Didelphis (Metachirus) nudicaudatus* GEOFF.

Body white, attenuated at the extremities, especially at the caudal extremity of the females; greatest diameter just below the termination of the esophagus.

Cuticle.—Cuticle thick, smooth, without transverse striation or lines and longitudina-wings. The comparatively great thickness and impermeability of the cuticle make the embedding in paraffin for histological sections especially difficult.

Body walls.—The walls of the body are formed by muscular fields which are made up of 3 fibers of cells joined obliquely (fig. 2), as is observed in the majority of nematodes, but one of the fibers is incomplete as shown by the figure. In transverse sections these cells appear sub-quadrangular, having three nearly plane surfaces with the periphery strongly differentiated into muscular fibrillae, and a curved one with differentiation forming trabeculae which are fixed on the digestive tube or on other cells, that is, the external and lateral faces are strongly differentiated into contractile fibrillael The longitudinal fields are distinct and wide,

(1) It is not impossible that the North American speciess different from the South American.

especially the lateral fields, which may have a breadth equal to the muscular cells.

Excretory pore.—The excretory pore is situated near to the middle of the esophagus, at a distance of 1,044 to 1.0479 mm. from the anterior extremity, and is the termination of a narrow canal directed from within outward.

Nerve ring.—This is situated at the anterior part of the oesophagus, about 0,462 to 0,609 mm. from the anterior extremity.

Mouth.—Subtriangular, protected by three triangular lips, not very large and each one showing two distinct papillae. The lips measure about 0,049 to 0,056 mm. in length.

Vestibule.—Ample, comparable to that of the *Subulurinae*; on section it is trilateral or starshaped with three points and three invaginations or angles (fig. 7). It is strongly covered with chitin and the angles show numerous small teeth directed inward which increase in size from within outward (fig. 3). At the botton of the vestibule, guarding the entrance to the esophagus, are three subtriangular prominences which are homologous to those existing at the bottom of the buccal capsule of the *Triodontophorus*. The vestibule measures 0,106 to 0,156 mm. in depth.

Esophagus.— Constituted by the esophagus properly speaking and by a voluminous subspherical bulb. The esophagus properly speaking is rigid and subspherical, and presents the last portion slightly dilated, forming something like an outline of a second bulb, as seen in the *Kathlanidae*. The walls of the esophagus are strongly muscular, appearing to be formed of three series of cells whose protoplasm is almost entirely differentiated into radially disposed muscular fibrillae. The cavity is very curious and is trilateral on section, there being three branches which start from a central portion and widen outwards. This cavity is lined by a strong chitinous cuticle, as can be seen in figures 7 to 10, the central parts being obliterated by a structureless substance, so as to leave as free cavity only three ducts of semilunar transverse section (Fig. 8).

These ducts fuse at the height of the vestibule and near the terminal portion where the obliterating substance of the central portion becomes progressively reduced, and the lateral diverticula diminish until reduced to the form of a threepointed star, when seen in transverse sections (fig. 9.).

The esophagus properly speaking measures 1,044 to 1,914 mm. in length by 0,104 to 0,121 mm. in diameter.

The bulb, which begins immediately after the esophagus properly speaking, is subspherical and has the same structure as the esophagus, the internal lining being much thicker, and differentiated into three strong, chitinous valves with longitudinal grooves. The diameter of the bulb is from 0,313 to 0,481 mm. (Fig. 10).

Intestine.—Following on the esophageal bulb is found the intestine, which, for convenience of study and on account of its very complex structure, we will divide into the following parts: 1) cecum; 2) first portion; 3) midportion; 4) terminal portion; 5) rectum.

The cecum or intestinal diverticulum (Fig. 9, 10 is a portion of the intestine which is prolonged parallel to the esophagus on the ventral side. This cecum, which measures from 0,957 to 1,218 mm. in length, is fingershaped, more or less cylindrical, and has a pronounced flattening in the region of the esophageal bulb to accomodate itself between this organ and the body wall. The structure of its walls is simple, of moderate thickness, with ample cavity, as can be seen in figure 9 and 10.

The appearance of the walls of the intestinal diverticulum is similar to that observed in the midportion of the intestine. The opening into the intestine is ample, the cecum forming an intestinal prolongation without sharp transition.

The first part of the intestine follows on the esophagus and intestinal diverticulum; it is the most voluminous part of the digestive tube. The part in contact with the esophageal bulb and with the beginning of the

cecum has thick walls with voluminous cavity but soon the walls take on a very curious appearance. There appear in the interior voluminous prominences or villosities, which may be seen externally as dark blotches. These prominences, which almost reach the middle of the cavity, are few in number and give the cavity a very irregular outline when observed in transverse sections. The portion thus differentiated is clearly observable in the male specimens (Fig. 1), but in the females it is usually obscured by the coils of the oviduct and ovary. This first portion of the intestine measures about 1,21 to 1,56 mm. in length.

The midportion of the intestine has the usual structure of the intestine of small nematodes, is more or less circular in section (Fig. 11), and constitutes the greater part of the digestive tube.

The terminal portion is easily observable in the females while in the males it is more or less involved with the deferent canal and ejaculatory duct, ventrally, and with the sheath of the spicules, dorsally. The cavity is filled with villosities that are less notable than those seen in the first portion, but in greater number and directed from before backward. This villous portion is about 1,2 mm. in length and narrower than the anterior villous portion and terminates in the rectum.

The rectum, which is the last portion of the intestine, is narrow with strongly chitinized walls, and terminates in the females (Fig. 6) in a transverse anus, and in the males in a common cloaca with the ejaculatory canal and the sheaths of the spicules. On account of the proximity and consequent complication of the male genital organs, it is not easily observable in the individuals of this sex. In the females, on the contrary, it can be observed entirely, since the uterine and ovarian coils are always much above. The rectum, in the female, is provided with four large monocellular glands.

Female genital apparatus. – The vulva is situated just above the middle of the body. It is formed by a transverse slit with slightly projecting lips. In the fecundated females it is generally found protected by a shield of brown color, formed by the copulation cement.

The ovijector is of a very simple type, claviform, with the extremity in opposition to the rounded vulva, from which start two thin and muscular vestibules. The ovijector (Fig. 12) is directed forward and measures about 1,2 mm. in length (without the vestibules) by 0,087 to 0,190 mm. in diameter, (minimum and maximum). The vestibules measure 0,240 by 0,070 mm. and are cylindrical. The uteri are divergent, almost straight and contain a large number of eggs in various stages of development. In continuation with the uteri are the oviducts, which are at first of normal appearance and of regular diameter, and later show an irregular outline of moniliform appearance and much reduced diameter, which the eggs pass with difficulty. The oviducts are coiled near the termination of the ovaries, the anterior being at a short distance from the esophagus, at the height of the anterior differentiated portion of the intestine and the posterior in front of the terminal differentiated portion of the intestine. The initial part of the uterus and the not moniliform portion of the oviduct act as a seminal receptaculum, the fecundation occurring in the oviduct.

The ovary following close on the oviduct, very long and cylindrical. It forms some coils in the part near the oviduct and then has its course in opposition to the uterus of the same side, making many convolutions and crossing with the opposite ovary at about the height of the vulva, such belonging to the amphidelphous type of SEURAT.

Ova. – Relatively large, of ellipsoid form, with a thick and rugose shell including an embryo at the time of being deposited; they measure about 0,120 mm. in length by 0,056 to 0,063 mm. in greatest diameter.

Male genital apparatus. – It is formed of a cylindrical testicle, short and curved in U shape, its terminal branch being the

shorter. The convexity of the U is pointing to the anterior extremity, and very distant from the termination of the esophagus; about at the beginning of the first portion of the intestine. Next to the testicle is a voluminous deferent duct wich also has the function of a seminal vesicle. Just at the initial por tion of the deferent canal there is a pair of small diverticula branched into three or four fingerlike prolongations, which in the old males are full of spermatozoids and seem to have also a glandular function. (Fig. 1). The deferent canal terminates in an claviform ejaculatory duct with muscular walls which measure about 0,8 mm. in length. The spicules (Fig. 1, 4, 5) are subequal, winged, and partly rugose, the rugosities of light colour are seen only in specimens well cleared in phenol. The spicules measure about 0,870 to 1,165 mm. in length. The gubernaculum is flat, subtriangular when seen from the front, and in the form of a comma when seen in profile; it measures about 0,197 to 0,243 mm. in length. The caudal extremity of the males (Fig. 4 and 5) has the ventral surface differentiated and the cuticle rugose for about 1,3 to 1,7 mm.; it is curved in an are and internally has muscles obliquely directed from the median ventral field to the lateral fields, as observed in the *Kathlanidae*.

In the same specimens the roughened portion is slightly excavated, appearing to form an ample ellipsoid cup with distinct borders.

The papillae of the caudal extremity are disposed in three groups with three pairs of papillae in each (Fig. 1, 4 and 5).

The first group is postanal, and the papillae are very small, not arranged in line, and support a very small lateral wing. The second group is adanal and disposed in a straight line, oblique to the lateral fields; the papillae are larger than those of the first group, very near to each other and equidistant. The third group is preanal, the papillae are large, equidistant, arranged in a straight line parallel to the lateral fields and widely separated one from the other.

Habitat. — This parasite is found exclusively in the large intestine, and especially the cecum of the gambás *(Didelphis)*; we have material from the following places: Manguinhos, Angra dos Reis, collected for us by Dr. GOMES DE FARIA; São Paulo, collected by Drs. FLORENCIO GOMES, CARINI, MACIEL and LUTZ in *D. aurita* and in São Paulo from *D. nudicaudatus*, collected by LUTZ.

It is very common in the gambás where it generally exists in large numbers.

Vorbemerkungen zum Studium der Entwicklungsgeschichte brasilianischer Trematoden

von

DR. ADOLPHO LUTZ.

Ich beabsichtige in dieser Leitschrift ueber Studien zu berichten, welche ich in den letzten Jahren ueber die Entwicklungsgeschichte zahlreicher hiesiger Trematoden anstellte; letztere stammten zum kleineren Teile von auswaerts, meist konnten sie in der Naehe des Institutes in genuegender Menge gesammelt werden. Zu besserem Verstaendnis dieser Mitteilungen, sende ich einige Bemerkungen voraus, welche sich auf die verschiedenen Entwicklungsstufen und die bei ihrem Studium angewandten Methoden beziehen, wobei besonders neue oder wenig bekannte Punkte betont werden sollen. Die allgemein bekannten Tatsachen koennen in jedem Lehrbuche der Zoologie oder Parasitologie gefunden werden und sollen nur gelegentliche Erwaehnung finden.

Die Zahl der in Brazilien gefundenen und von fremden Autoren studirten Trematoden ist schon ziemlich gross. Noch zahlreicher sind die benannten, aber bloss oberflaechlich beschriebenen Arten. Es gibt auch eine, noch ziemlich beschraenkte Zahl von brasilianischen Arbeiten. Wie zu erwarten stand, hat sich auch dieser Teil der einheimischen Fauna als reich und mannigfaltig erwiesen. Es geht dies schon aus den zahlreichen von NATTERER gesammelten und grossenteils den erwaehnten Arbeiten zu Grund liegenden Arten hervor.

Auf der anderen Seite herrscht tiefes Schweigen ueber die Entwicklungsgeschichte dieser Arten, sowohl in der auslaendischen, wie in der einheimischen Litteratur. Zur Zeit erinnere ich mich nur an die von PIRAJÁ gegebene Beschreibung der *Cercaria Blanchardi* (die wahrscheinlich zu *Schistosomum Mansoni* gehoert) und an diejenige einer *Tetracotyle* aus Venezuela. Beide Arbeiten beschraenken sich auf die Beschreibung, ohne die Entwickungsgeschichte der Parasiten zu beruehren.

Es ist bereits an der Zeit, etwas auf dieses Kapitel einzugehen, das wichtiger ist, als die blosse Beschreibung neuer Arten. Die Erforschung der verschiedenen Vorstufen der Entozoen ist nicht nur fuer die Prophylaxis von groesster Wichtigkeit, sondern auch rein wissenschaflich von groesstem Interesse. Es gibt nichts anziehenderes, als die Feststellung der verschiedenen Entwicklungsgaenge, welche durch Wirtswechsel komplizirt und durch die merkwuerdigsten

Anpassungen beguenstigt werden. Ausserdem sind sie von groesster Bedeutung fuer die Kontrolle des Wertes der neueren systematischen Einteilung dieser Parasiten.

Es ist bekannt, dass alle digenetischen Trematoden einen Teil ihrer Entwicklung in Mollusken durchmachen, speziell in solchen, die in Suesswasser oder im Meere leben. Letztere sind die ersten Wirte fuer Parasiten der Seefische und Meeresvoegel. Landschnecken koennen zwar unter besonderen Bedingungen die ersten Wirte von Trematoden sein, die spaeter auf Saeugetiere oder Voegel uebergehen, aber solche Faelle scheinen verhaeltnissmaessig selten. Seeschnecken und -muscheln sind artenreich und oft schwer zu beschaffen, was die Loesung der Entwicklungsprobleme fuer die Trematoden der Seefische und -voegel erschwert. Dagegen ist die Artenzahl bei den Suesswassermollusken mehr beschraenkt und deren Beschaffung gewoehnlich leicht. Nach Ausschluss einiger selten oder nie infizirten Arten, bleibt eine beschraenkte Zahl, nach welcher zahlreiche Trematoden convergiren, die sich im erwachsenen Zustande ueber eine grosse Reihe der verschiedensten Wirte verteilen. So koennen einige der gewoehnlichsten und massenhaft auftretenden Suesswasserschnecken als Wirte fuer eine groessere Zahl von Trematodenart dienen, von denen mehrere in demselben Individuum vorkommen koennen. Parasitenmaterial, das auf den ersten Blick nur einer Spezies anzugehoeren scheint, laesst dann bei genauerer Untersuchung zwei bis drei verschiedene Arten unterscheiden. Diess ist namentlich bei den inzystirten Formen der Fall.

Untersuchung der Suesswassermollusken.

Es erscheint zweckmaessig diese Studien nit der Untersuchung von Suesswasserschnecken zu beginen, die man leicht lebend beobachten kann. Bringt man viele Exemplare derselben Art mit wenig Wasser an die Sonne, so kann man oft in kurzer Zeit das Ausschwaermen zahlreicher Cercarien bewirken. Durch Isolirung kleinerer Gruppen, gefolgt von einer solchen der Individuen, welche eine infizirte Gruppe bilden, kann man in kurzer Zeit die Individuen bestimmen, welche Partheniten (Redien oder Sporocysten) enthalten. Erhaelt man diese am Leben, so verfuegt man waehrend laengerer Zeit ueber ein reichliches Cercarienmaterial.

Die Beobachtung lebender Individuen gestattet indessen nicht, ihre Infektion mit Trematoden auszuschliessen. Nicht nur die noch unreifen Partheniten muessen direkt aufgesucht werden, sonderne auch die Cerkarien werden bei manchen Arten zurueckgehalten und gelangen erst nach dem Tode des Wirtes ins Freie. So geschieht es z. B. bei dem Lebegel.

Feststellung der Zwischen- und endgiltigen Wirte.

Der zweite Wirte ist seltener der definitive, wie z. B. bei dem Genus Schistosomum; gewoehnlich fungirt er nur als Zwischenwirt. Er wird durch Versuche mit Cercarien ermittelt und ist besonders unter Mollusken, Crustaceen, Insektenlarven, Wuermern, Kaulquappen und Fischen zu suchen. Bringt man solche in das cercarienhaltige Wasser, so kann man die Infektiou entweder direkt beobachten oder durch nachtraegliche Untersuchung feststellen. Die Versuchstiere muessen entweder im Laboratorium gezuechtet sein oder durch ihre Herkunft gestatten, eine bereits bestehende Infektion auszuschliessen. Bei Cercarien, die im Freien Cysten bilden, sucht man solche nach einigen Stunden, falls man die Incystirung nicht direct beobachtet hat. Es empfiehlt sich fuer solche Versuche kleinere Glasgefaesse zu verwenden, welche gestatten den Versuch bei schwacher Vergroesserung direkt unter dem Mikroskope zu verfolgen.

Nach dem Eindringen in den zweiten Wirt, incystiren sich viele Cercarien sofort. Andere bleiben einige Tage beweglich, bevor sie Cysten bilden. In beiden Faellen entwickeln sie sich waehrend einiger Zeit weiter, ohne aber die voellige Reife zu erlangen. Deswegen sollten die Versuche, den Endwirt festzustellen, erst einige Tage nach

der Infektion des Zwischenwirtes unternommen werden. Manchmal gestattet die Organisation der in den Zwischenwirten gefundenen Trematoden einen Schluss auf den Endwirt, weil sie Aehnlichkeiten mit den aus solchen Endwirten bekannten Arten zeigt; indessen wird der sichere Beweis erst durch das helminthologische Experiment geliefert. Die Resultate desselben sind oft ueberraschend und fuehren nicht selten zur Entdeckung neuer Arten.

Bestimmung der erwachsenen Trematoden und ihrer Endwirte.

Nach Feststellung eines zweiten Wirtes, der nicht definitiv ist, sucht man den Endwirt. Derselbe ist ein Tier, welchem der Zwischenwirt als Nahrung dient und zwar im Wasser oder auch ausserhalb desselben, wenn es sich um eine Kaulquape oder Insektenlarve handelt. Die Parasiten solcher gehen, im letzten Falle, in das gefluegelte Insekt ueber, welches von einer Fledermaus, einem Vogel oder auch von einem Batrachier gefressen werden kann. Ist der Zwischenwirt eine Quappe oder ein Fisch, so suche man den Endwirt unter Tieren, welche Kaulquappen, Froesche, Kroeten oder Fische fressen, wie groessere Fische, Schlangen, Voegel und eventuell Saeugetiere. Die frei gebildeten Cysten inficiren namentlich Voegel und Saeugetiere, Pflanzenfresser inbegriffen.

Nachdem man an einer bestimmten Lokalitaet das Vorkommen von Cercarien festgestellt hat, empfiehlt es sich zu erforschen, welche Tiere an derselben vorkommen. Handelt es sich um kleinere Gewaesser, so kommen von Wirbeltieren vorzugsweise in Betracht: zuerst Amphibien, dann kleine Fische und zuletzt wasserliebende Schlangen; Voegel und Saeugetiere finden sich vorzugsweise an groesseren Gewaessern.

Bei solchem Forschungen stuetzt man sich sowohl auf fruehere eigene Beobachtungen, als auch auf die in der helminthologischen Litteratur enthaltenen Angaben. Unsere Arten werden jedoch nur ausnahmsweise mit europaeischen und nordamerikanischen uebereinstimmen, meistens nur, wenn die Wirte Haustiere oder vom Menschen eingefuehrt sind, da die neotropische Fauna ziemlich scharf abgegrenzt ist. Allerdings machen die parasitischen Trematoden in so fern eine Ausnahme, als sie einige Arten mit der europaeischen und nordamerikanischen Fauna teilen; haeufiger finden sich nur kleine Differenzen mit den typischen Formen, selbst wenn die Wirte ganz verschieden sind. So sind die Trematoden der brasilianischen Froesche teils identisch, teils wenig verschieden von den europaeischen und nordamerikanischen, waehrend die Wirte sehr verschiedenen Gattungen oder wenigstens Arten angehoeren. Die Mollusken, welche die ersten Wirte sind, gehoeren ebenfalls zu anderen Arten, aber zu denselben Gattungen und solche verwandte Species koennen einander ersetzen, was auch fuer die Endwirte der Trematoden gilt. So werden auch die zahlreichen Trematoden des eingefuehrten zahmen Gefluegels grossenteils die noetigen Bedingungen fuer die Erhaltung ihrer Art finden. Es ist daher natuerlich, dass ein grosser Teil meiner Beobachtungen sich auf mehr oder weniger bekannte Formen bezieht. Unsere Kentnisse ueber die Biologie der Trematoden sind aber so fragmentarisch, dass die vollstaendige Entwicklung nur fuer eine ganz geringe Zahl von Arten bekannt ist, waehrend fuer viele gemeine Parasiten der Haustiere die Entwicklungsgeschichte zum groessten Teile unaufgeklaert ist. Desshalb muss jeder Beitrag zur Loesung dieser Probleme von groesstem Interesse sein. Dass unsere Kenntnisse ueber diessen Gegenstand noch os wenig vorgeschritteu sind, beruht nicht nur auf der geringen Zahl der Beobachter, sondern auch auf den inhaerenten Schwierigkeiten, zu deren Ueberwindung lange Vorstudien, viele Zeit, genuegend Geduld und etwas Glueck beim Aufsuchen des Studienmateriales noetig sind.

Aufsuchen dar Trematoden in den Endwirten.

Wenn man in einer gegebenen Gegend

die facultativen Endwirte festgestellt hat, setzt man sich in den Besitz lebender oder toter Exemplare, um die in denselben vorkommenden Trematoden zu bestimmen. Es ist immer gut, zuerst die Faezes zu mikroskopiren, um eventuell vorhandene Trematodeneier festzustellen. Dieselben kennzeichnen sich durch das Vorkommen eines, nur selten fehlenden, Deckels an einem der beiden Pole. Sie zeigen gewoehnlich Eiform, doch beobachtet man in eingen Faellen fadenfoermige oder dornartige Fortsaetze der Schale. Die Farbe der Eischale wechselt, je nach der Art, von wasserklar, gelblich oder gelb bis dunkelbraun und nahezu schwarz. Im Innern findet sich eine Dottermasse, die eine Eizelle umschliesst, oder auch ein schon fertiger Embryo, welche oefters zwei, vereinigte oder getrennte, stark pigmentirte Ocellenflecke aufweist.

Die aufgefundenen Eier koennen von Darmtrematoden stammen; doch gehen auch die Eier der in den Luftwegen oder Lungen lokalisirten Arten mit den Faezes ab. Auf der anderen Seite gibt es zahlreiche, besonders kleinere Species, deren Eier nicht in den Abgaengen aufzufinden sind, weil der Wurm mit dem ganzen Vorrat fertiger Eier abgeht, die groesstenteils erst nach dem Tode desselben frei werden.

Auch beim toten Tiere empfiehlt es sich, den Inhalt der letzten Darmpartie auf Eier zu untersuchen. Dann untersucht man methodisch den ganzen Darmkanal, die Luft-and Harnwege, die Gallenblase, die Leber und das Pancreas. Hat man Eier beobachtet, so muss man auch erwachsene Trematoden finden, die aber sehr klein, selbst mikroskopisch sein koennen.

Hat man Trematoden gefunden, so verbleicht man ihre Eier mit den in den Faezes geobachteten. Enthalten sie noch keinen Embryo, so bleiben sie bis zur Bildung desselben bei Zimmertemperatur in Incubation, nachdem man sie durch Auswaschen isolirt hat. Man haelt sie in einer feuchten Kammer oder unter einer duennen Wasserschicht. Der fertige Embryo gleicht den in embryonenhaltigen Eiern gefundenen Formen.

Entwicklung und Ausschluepfen des Embryos oder Miracidiums und Eindringen in den ersten Wirt.

Zum Ausschluepfen des Embryos ist Licht uud Waerme noetig und deshalb verlassen sie die Schale nicht, solange die Kulturen dunkel gehalten werden. Bringt man sie ploetzlich an die Sonne, so sieht man oft nach kurzer Zeit zahlreiche Miracidien in lebhafter Bewegung. Manchmal erfolgt das Ausschluepfen nicht, sei es das die Embryonen nicht genuegend reif sind, sei es das sie die Schalen erst verlassen, nachdem sie von dem ersten Wirt verschluckt wurden, der, wie immer, zu den Mollusken gehoert.

Um diesen Wirt zu bestimmen, bringt man reife Eier oder Miracidien in ein Uhschaelchen und fuegt verschiedene Suesswassermollusken in kleineren Exemplaren hinzu. In einigen Faellen sieht man die Embryonen direkt die Haut der Schnecken durchsetzen; in anderen Faellen werden sie erst verschluckt oder aspiriert und dringen dann durch die inneren Membranen des Atmungs- oder Ernaehrungssystems ein. Nach dem Eindringen verwandeln sich die Miracidien in Sporocysten, die schwer zu beobachten sind, bevor sie sich vermehren. Sie bringen aber neue Generationen von Sporocysten und Redien hervor, in welchen, nach ungefaehr Monatsfrist, zahlreiche Cercarien auftreten. Man findet dann die Sporocysten und Redien ohne Schwierigkeit, gewoehnlich in der Leber oder der Geschlechtsdruese, manchmal auch in der Niere und in den Kiemen der Mollusken; die Cercarien findet man am selben Ort und nach dem Ausschwaermen frei im Wasser.

Es ist wichtig zu wissen, dass die Miracidien selten gleich nach dem Verlassen der Eischalen einzudringen versuchen; gewoehnlich folgt erst eine Periode der Indifferenz, waehrend welcher die Confrontation von Miracidium und Schnecke nicht zu dem erwarteten Resultate fuehrt. Mangelnde Kenntniss dieser Tatasache erklaert manche Misserfolge sonst gut angelegter Versuche.

Entwicklung der Miracidien in den ersten Wirten.

Selbst unter den abnormen Versuchsbedingungen ist die Zahl der eingedrungenen Miracidien gewoehnlich klein. Sie verwandeln sich bald in junge Sporocysten; nur bei einigen *Monostomum*-Arten bringen sie eine kleine, aber gut charakterisirte Redie hervor, die schon im Miracidium enthalten ist. Junge Sporocysten sind schwer zu finden, da ihre Lokallsation gewoehnlich unsicher ist und sie selbst wenig differenziert sind. In der Regel ist es bequemer, die Bildung neuer Parthenitengenerationen abzuwarten, die besser charakterisirt sind. Die Sporocysten sind meist so einfach gebildet, dass sie sich kaum durch Farbe, Form und Groesse unterscheiden. Die Redien sind mehr differenzirt, doch erlauben sie selten, die Art zu bestimmen. Erst wenn die Cercarien auftreten, wird dies leichter. Die massenhafte Produktion der letzeren kompensirt die enormen Verluste an Eiern, Miracidien und Cercarien, von denen nur der kleinste Teil die noetigen Bedingungen zur Weiterentwicklung findet. Die Cercarien unterscheiden sich leicht, nicht bloss durch die Struktur des Koerpers, sondern auch durch die aeusserste Mannigfaltigkeit des Schwanzanhangs, der gestattet, sofort eine groessere Anzahl von Gruppen zu unterscheiden. In diesen kennzeichnen sich die Arten durch Form und Groesse, sowie durch die Groesse und Zahl der Saugnaepfe, die Bildung des Exkretionsapparates und andere Eigentuemlichkeiten der Struktur. Die Organisation ist schon ziemlich kompliziert, aber schwer zu erkennen, weil Gewebe und Organe einen Embryonalcharakter zeigen und die Zellen sich wenig von einander unterscheiden. Von dem Genitalapparate existiren nur undeutliche Anlagen, wenn dieselben nicht ganz fehlen. Immerhin gestattet die Anwendung von Immersionslinsen, bei genuegender Geduld manche Einzelheiten zu erkennen, die Anfangs nicht sichtbar sind. Einige Autoren scheinen ueber eine besondere Geschicklichkeit zu verfuegen, mit welcher sie Strukturen erkennen, die fuer den gewoehnlichen Beobachter nicht sichtbar sind. Dies erklaert sich durch grosse Sehschaerfe, spezielle Kentnisse und viel Geduld; vielleicht spielt manchmal auch die Phantasie etwas mit. Jedenfalls werden die bestehenden Strukturen spaeter deutlicher, wenn es gelingt, die Weiterentwicklung zu verfolgen, die in einem neuen Zwischen oder Endwirte stattfindet.

Klassifikation der Cercarien.

Zum Zweck des Studiuns der Cercarien empfehlt es sich, dieselben zu klassifiziren und zu benennen; Klassifikation und Namen sind allerdings nur provisorisch. Letztere werden aber definitiv, wenn sich herausstellt, dass die erwachsenen Formen noch unbekannt waren. Der allgemeinen Praxis zufolge, stuetzt sich die Klassification auf die ausgewachsenen Tiere; doch koennen auch die frueheren Zustaende beruecksichtigt werden.

LUEHE stellte eine Einteilung der Cercarien auf, die ich, mit einigen Anmerkungen in der Form anfuehre, wie sie CORT (1915) wiedergab: dieselbe genuegt fuer den praktischen Gebrauch.

A. Cercarien von *Gasterostomum*:
   Hinterende mit zwei langen Anhaengseln. Mund in der Mitte der Bauchflaeche. Darm einfach, sackfoermig. Beispiel: *Bucephalus polymorphus*.

B. Cercarien von *Monostomiden*:
   Acetabulum fehlt.

C. Cercarien von *Amphistomiden*:
   Acetabulum am hintern Koerperende.

D. Cercarien von *Distomiden*:
   Acetabulum vor dem Hinterende.

LUEHE stellt in erste Reihe die *Lophocercarien* mit der einzigen Species *Lophocercaria cristata* LA VALETTE, bei der das Acetabulum fehlt und der Mundsaugnapf stark veraendert erscheint. Ich halte es fuer nahezu sicher, dass dieselbe zu *Gigantobilharzia* oder einer ganz nahe stehenden Form gehoert. Sie kann deshalb als eine abwei-

chende Form zu den *Distomiden* gestellt werden.

Die *Holostomiden* fehlen in dieser Einteilung, da LUEHE, wie fast alle neueren Autoren, eine direkte Entwicklung ohne *Partheniten* annahm. Ich halte diese Annahme fuer irrig und habe bereits in einer vorlaeufigen Mitteilung erwaehnt, dass dieselben aus gabelschwaenzigen Cercarien hervorgehen.

Ich gebe jetzt eine Einteilung der Cercarien der Distomiden in Schluesselform:

Schluessel fuer die Bestimmung der Distomidencercarien:

1. Isolirte Cercarien..... 2
   Cercarien am Schwanzende verbunden....
   Cercariae symphytocercae
2. Schwanz gut ausgebildet..... 4
   Schwanz stummelfoermig oder fehlend.. 3
3. Schwanz stummelfoermig.....
   Cercariae microcercae
   Schwanz fehlend..... *Cercariaea*
4. Schwanz unbehaart.. 5
   Schwanz mit seitlichen Haaren.....
   Cercariae trichocercae
5. Schwanz einfach..... 6
   Schwanz gabelformig.
   Cercariae dicranocercae
6. Schwanz von maessiger Groesse..... 8
   Schwanz ungewoehnlich dick..... 7
7. Koerper in die Schwanzbasis zurueckziehbar.....
   Cercariae cystocercae
   Nicht zurueckziehbar. Schw. lang und dick.
   Cercariae rhopalocercae
8. Cercarien am Vorderende bewaffnet oder mit Kragen..... 9
   Kopf unbewaffnet....
   Anoplocercariae
9. Kopfende mit Stilet...
   Xiphidiocercariae
   Kopfende mit Kragen und Stachelhalsband
   Echinocercariae
   (Das Stachelhalsband ist meist undeutlich oder tritt erst in der Cyste auf).....

Ich ersetze die unkorrekte Bezeichnung *furcocercae* durch *dicranocercae* und sage statt *Rattenkoenigcercarien Cercariae symphytocercae.*

Symphytocerce und *trichocerce* Cercarien sind rar und wurden meist im Plankton gefunden. Es kann daher nicht befremden, dass ich dieselben nicht beobachtet habe. Von den andern Gruppen sind mir *microcerce Cercarien* und *Cercariaeen* nicht vorgekommen, wenn man nicht die *Leucochloridien* zu letzteren rechnen will. Ich werde die beobachteten Gruppen rasch besprechen:

Von *Cercariae dicranocercae* habe ich ca. ein Dutzend Arten beobachtet, deren erste Wirte zu wenigstens fuenf Gattungen von Suesswassermollusken gehoeren. Sie verteilen sich auf mehrere verschiedene Gruppen, die unter sich nicht naeher verwandt sind. Manche gehoeren zu *Holostomiden* und wenigstens eine zu den *Schistosomiden.*

Von *Rhopalocercarien* fand ich eine sehr interessante Spezies in *Semisinus* und eine kleinere in *Planorbis.* Letztere gehoert zu den *Echinostominen* und zwar zu *Mesorchis* oder *Monilifer.*

Zu den *Anoplocercarien* gehoeren die Cercarien von *Fasciola hepatica*, die in einer hiesigen *Limnaeusart* gefunden wurden, ferner kleine *Cercarien* aus *Hydrobia (Paludestrina)*, die in Brackwasser leben. Letztere gehoeren teils zu *Ascocotyle*, teils zu *Levinseniella.*

Die *Xiphidiocercarien* werden am haeufigsten gefunden. Ich kenne solche aus *Limnaeus, Physa, Planorbis, Spirulina, Semisinus* und *Ampullaria.* Sie gehoeren zu zwei Gruppen, zusammen mit ca. 10 Arten.

Echinocercarien sind ebenfalls sehr haeufig. Ich fand sie in *Limnaeus*, *Planorbis*, *Spirulina*, *Physa*, *Ampullaria* und *Semisinus*, manchmal schon incystirt und dann leichter zu erkennen. Andere Arten incystiren sich in Fischen und Kaulquappen.

Die *Cercaria cystophora* von *Halipegus ovocaudatus* oder einer nahe verwandten Art fand ich mehrmals in *Planorbis confusus*.

Die von mir im Cercarienzustand beobachteten Arten belaufen sich auf ueber dreissig.

Man kann die Cercarien auch nach den *Partheniten (Sporocysten* oder *Redien)*, in welchen sie gebildet werden, einteilen. Vollkommene Redien haben ein Organ, das bald als Mundsaugnapf, bald als *bulbus pharyngens* angesprochen wird und einen sackfoermigen Darm von verschiedener Laenge; am Kopfende findet man meist einen Kragen und am Hinterende zwei Fortsaetze, die der Bewegung dienen und bei jungen Redien deutlicher sind. Eine Geburtsoeffnung wird nicht sehr haeufig beobachtet. Redien, besonders juengere, bewegen sich oft lebhaft. Die Sporocysten sind rundliche, ovale oder schlauchfoermige Saecke, die ausser den Keimzellen nur wenig Struktur zeigen und meist unbeweglich sind. Zwischen diesen Extremen gibt es Uebergaenge. Die Redien verlieren, wenigstens im erwachsenen Zustande, nicht selten den Kragen, die Gehfortsaetze und die Beweglichkeit; auch der Darm und das in diesen fuehrende Organ koennen undeutlich werden. Andererseits koennen die Sporocysten sich stark verlaengern und beweglich werden, was zu Verwechslungen gefuehrt hat. Indessen gestattet eine sorgfaeltige Untersuchung die Bestimmung der Partheniten.

Bei den von mir beobachteten Arten entwickeln sich die *Xiphidiocercarien* immer in kurzen oder maessig langen Sporocysten; die *Dicranocercarien* entstehen in langen und beweglichen Sporocysten, eine mit Augenflecken versehene Gruppe jedoch in richtigen Redien. Die meisten anderen Cercarien entstehen in Redien, welche Unterschiede zeigen, die aber fuer eine Klassification kaum genuegen.

Von anderen Trematoden zeigen auch die *Monostomiden* die Redienform, die fuer den urspruenglichen und vollkommeneren Zustand gelten kann, waehrend die Sporocysten der bei Parasiten haeufigen Degeneration entsprechen.

Auch die Redien entstehen zuerst in einer Sporocyste, welche dem eingedrungenen Miracidium entspricht. Nur bei manchne *Monostomiden* enthaelt bereits das Miracidium eine Redie, die leicht zu erkennen ist. Durch ein von mir aufgefundenes Verfahren kann man dieselbe aus den Miracidien ausschluepfen lassen und sie erscheint dann trotz ihrer Kleinheit sehr deutlich und lebhaft beweglich.

Beobachtungen an Cercarien.

Ich finde, dass die Cercarien in der Regel nicht waehrend der Nacht auswandern. Das Ausschwaermen wird durch Licht und Waerme beguenstigt. Das besonders geignete Sonnenlicht kann man durch elektrisches oder diffuse Beleuchtung ersetzen und die Temperatur laeest sich auf mancherlei Weise erhoehen.

Im allgemeinen nimmt man an, dass der Cercarienschwanz besonders fuer die Locomotion diene. Dafuer eignet er sich indessen nur wenig und die Cercarien legen, auf Kosten einer anscheinend uebertriebenen mechanischen Arbeit, nur geringe Strecken zurueck. Die Miracidien erzielen nur mittelst ihrer Cilien ein relativ guenstigeres Resultat. Man muss sich indessen vergegenwaertigen, dass bei vielen, wohl den meisten Cercarien diese Bewegungen einem anderen Zwecke dienen, indem sie die Aufmerksamkeit der zweiten Wirte erregen, welche die Cercarien als gute Beute betrachten. In der Tat ueberzeugt man sich leicht, dass Agrionidenlarven, Kaulquappen und kleine Fische oft grosse Mengen von Cercarien verschlucken. Ich fand einmal eine Froschlarve, welche waehrend eines Versuches so viele Dicranocercarien verschluckt hatte, dass

ein Darmabschnitt mit solchen vollgepfropft war, wobei dieselben noch bestaendige und energische Bewegungen zeigten. *Bucephalus* und *Rhopalocercarien* erinnern an sich bewegende Dipterenlarven und werden von Fischen, wie diese, aufgeschnappt.

Ich gelangte nach und nach zu dem Schlusse (den ich in der einschlaegigen Litteratur nirgends erwaehnt finde), dass die Cercarien groesstenteils in ihre Wirte nicht von aussen eindringen, sondern von den inneren Membranen, nachdem sie zuerst verschluckt oder aspirirt wurden. Dies gilt als Regel fuer alle Arten, die in Insektenlarven eindringen; die Cysten derselben werden immer in der Naehe des Darms gefunden. Bei Kaulquappen und manchen Mollusken ist die Haut so weich, dass sie von einigen Cercarien ohne Schwierigkeit durchsetzt wird, doch dringen auch hier die meisten auf anderem Wege ein. Innere Hohlraeume, welche der Respiration dienen, wie die Mantelhoehle gewisser Mollusken und das Rectum der *Aeschniden*, bilden den Angriffspunkt fuer Cercarien, welche mit dem Wasser aspirirt werden.

Das Eindringen durch die Haut, wie es bei den *Schistosomiden* beobachtet wird, ist ein seltenes Vorkommniss, welches eine besondere Anpassung bedingt. Ueberdies findet auch hier die Einwanderung oft durch die Schleimhaeute statt.

Die hier besprochenen Verhaeltnisse erklaeren, warum bei Infektionsversuchen die Resultate unsicher sein koennen, selbst wenn die Versuchsbedingungen vollkommen guenstig zu sein scheinen.

Incystirung der Cercarien.

Einige Cercarien incystiren sich sofort an dem ersten Koerper den sie finden. So bilden diejenigen der *Fasciola hepatica* ihre Cysten auf dem Objecttraeger oder in dem Uhrschaelchen, die dem frisch geoeffneten ersten Wirte als Unterlage dienen und manche Monostomencercarien bilden zahlreiche Cysten auf dem Gehaeuse der Schnecke, in welcher sie entstanden. In solchen Faellen beginnt die Cystenbidung bald, dauert aber laengere Zeit, da die Cysten aus verschiedenen Schichten bestehen, welche ihr die noetige Dicke und Dichte verleihen.

Die meisten Cercarien incystiren sich in einem Zwischenwirte, der oft ebenfalls zu den Mollusken gehoert. Sie koennen sich dann nach dem Ausschwaermen wieder in demselben Weichtiere incystiren oder in einem zweiten derselben oder einer anderen Art. Viele Echinocercarien bilden ihre Cysten in Mollusken, andere ziehen Kaulquappen vor, in denen sie sich, je nach der Art, verschieden localisiren. Die Xiphidiocercarien, die ich beobachtete, incystiren sich meist in wasserbewohnenden Insektenlarven, seltener in Kaulquappen.

Im Zwischenwirte wird die Cyste um so schneller gebildet, als sie meist eine duenne Membran hat. Je nach der Art, ist sie rund oder oval, mit oder ohne Freilassung eines groesseren Raumes. Das Excretionssystem fuellt sich nach und nach mit koernigen Massen, die gewoehnlich aufgespeichert werden und durch ihre Lagerung und ihr Aussehen die aelteren Cysten charakterisiren. Manchmal kann man noch das Xiphidium im Innern erkennen, waehrend bei den Echinocercarien ein Stachelkranz auftritt oder deutlicher wird.

Auf diese Weise ist es moeglich, unter Beruecksichtigung der Lebensweise des Wirtes, die Gruppe und manchmal selbst die Art der Cercarien festzustellen, welche die Cysten gebildet haben.

Die eingeschlossene Trematodenlarve ist anfangs sehr beweglich wird aber spaeter ziemlich apathisch. Sie braucht kaum Nahrung, obwohl die Entwicklung noch fortschreitet. Selbst zahlreiche Cysten werden gut ertragen, wenn nur die Invasion sich auf laengere Zeit verteilt.

Man erhaelt die Cysten durch Versuche oder durch die Untersuchung spontan inficirter Wirte. Man findet sie haeufig in Mollusken, Insektenlarven, Kaulquappen und Fischen aus Gewaessern, an denen Wasservoegel leben, und in guenstigen Faellen, kann man den Endwirt erkennen, wenn man

festgestellt hat, welche Tiere sich dadelbst mit den Zwischenwirten ernaehren.

Die Eigenthuemlichkeiten, die man an den incystirten Trematoden nicht deutlich erkennen kann, lassen sich oft beobachten, wenn man die Cyste durch Compression zum Platzen bringt. Man braucht dazu reichliches Material, da das Verfahren unsichere Resultate ergibt. Mit kuenstlicher Verdauung laesst sich kaum mehr erreichen, wie mir zahlreiche Versuche gezeigt haben.

Feststellung des Endwirtes.

Die Feststellung der Endwirte erfolgt durch Fuetterungsversuche, welche sich auf wenige Experimente beschraenken koennen, wenn man einerseits die vorkommenden Cysten, andererseits die in der Lokalfauna nachweisbaren Trematoden kennt.

Man kann dabei auf verschiedene Weise vorgehen. Sind die Versuchstiere sicher trematodenfrei, so sucht man die erwachsene Form zu erhalten, wozu gewoehnlich drei bis sechs Wochen genuegen. Der Erfolg des Experimentes laesst sich oft durch Mikroskopiren der Faezes und Nachweis der Eier erkennen.

Die Zahl der erhaltenen erwachsenen Trematoden sollte der Zahl der verfuetterten reifen Cysten entsprechen. Dies ist auch tatsaechlich der Fall, wenn die Voraussetzung des gewoehnlichen Endwirtes richtig war. Wurde die Verfuetterung in Zwischenraeumen wiederholt, so sollen neben den vollkommen reifen auch entsprechend zahlreiche unreife Stadien gefunden werden.

Wenn es mir auch gewoehnlich nicht gelang, die Desincystirung durch kuenstliche Verdaung zu erreichen, so gelingt dieselbe doch meist, wenn man die Cysten einem geeigneten Tiere eingibt und nach zehn bis fuenfzehn Stunden untersucht. Selbst, wenn man nicht den gewoehnlichen Endwirt verwendet hat, kann man auf diese Weise oft ein befriedigendes Resultat erzielen.

Beurteilung der helminthologischen Versuche.

Die helminthologischen Probleme sollten durch den Versuch in entscheidender Weise geloest werden. Es finden sich indessen in der Praxis allerlei Schwierigkeiten und Fehlerquellen, weil manche Nebenumstaende unbekannt sind, welche das Resultat beeinflussen koennen. Deswegen ist ein einziger Versuch oft nicht genuegend, sondern es muss eine Wiederholung stattfinden. Die Resultate sollten unter gleichen Bedingungen konstant sein, sonst muss man eine Erklaerung dafuer suchen. Die vermeidung einer spontanen Infektion vor oder waehrend der Versuchszeit muss immer im Auge gehalten werden.

Die mechanische Arbeit beim Aufsuchen der gezuechteten Parasiten ist oft sehr gross, namentlich wenn es sich um mikroskopische oder ganz junge Formen handelt. Man muss deshalb die Versuchstiere moeglichst klein waehlen und vor der Versuchszeit die Nahrungszufuhr beschraenken.

So kann man bei kleinen Froeschen den ganzen Darm und die Lungen in einem mikroskopischen Praeparate untersuchen. Man verwendet dabei zweckmaessig statt der gewoehnlichen Objekttraeger und Deckglaeser groessere Glasplatten und-plaettchen. Durch Druck mit der unpolirten Kante eines Objekttraegers kann man den Ganzen Darminhalt, oft mit der Mukosa auspressen, worauf der uebrige Darmschlauch meits genuegend durchsichtig wird, um in toto untersucht zu werden. Die uebrigen Viscera und das Waschwasser muessen noch einmal untersucht werden, wobei man oft Parasiten findet, die der direkten Untersuchung entgingen. Man muss nicht vergessen, dass Trematoden ausser dem Darm in Lungen, Leber, Pankreas und Nieren, einschliesslich des zu- und abfuehrenden Kanalsystemes, in der Nasenhoehle und deren Ausbuchtungen, ja selbst in den Blutgefaessen gefunden werden koennen. Alles dies gilt auch fuer die wilden Tiere, deren Parasitenfauna festgestellt werden soll.

Wenn bei den Versuchstieren eine fruehere Infektion nicht ausgeschlossen werden kann, so macht man die Untersuchung bevor die Parasiten die voellige Reife erlangt haben. Findet man dann juengere Trematoden die nach Zahl und Entwicklung den verfuet-

terten Cysten entsprechen, waehrend eine Infektion kurz vor der Versuchszeit ausgeschlossen ist, so kann der Versuch als gelungen gelten. Die Geschwindigkeit der Entwicklung haengt vom Entwicklungszustande der verfuetterten Trematoden und von der Koerpertemperatur des Wirtes ab. Bei Kaltbluetern ist das Wachstum in den ersten Tagen sehr langsam, dagegen bei Voegeln rascher, als bei Saeugetieren. Die grossen und entwickelten *Clinostomum*larven gelangen schon drei Tage nach der Uebertragung auf Reiher zur Eibildung.

Einige Trematoden entwickeln sich in ganz verschiedenen Wirten, die sich in aehnlicher Weise ernaehren. Bei den meisten wird aber die voellige Reife nur im richtigne Wirte erreicht. Speciesunterschiede der Wirte sind in der Regel ohne Bedeutung, solange es sich um Repraesentanten derselben oder nahe verwandter Gattungen handelt.

Sur la lyse microbienne transmissible.

(Bacteriophage de d'Hérèlle).

par le

Dr. J. DA COSTA CRUZ

En 1917, d'Hérèlle communiquait á là Académie des Sciences, qu'il avait trouvé dans les selles de dysenteriques en convalescence, un microbe filtrant, parasite du b. SHIGA qui était capable de s'adapter au b. FLEXNER et Y dans les cultures mixtes.

Il remarquait en même temps que la présence de ce microbe qu'il a nommé plus tard "Bacteriophagum intestinale", coincidait en général avec l'amélioration des malades.

Quelques temps après cet auteur, trouvait des bacteriophages pour le B. Typhique, B. Paratyphique A et B et pour le b. proteus.

La technique employée, était des plus simples: On ensemencait les matières en bouillon Martin et après un séjour de 24 heures à 37º, on filtrait en bougie Chamberlain L2. Dans les filtrats éxistait alors, le virus capable de parasiter et dissoudre complètement en 24 heures la culture d'un des germes cités, même si on employait une quantité minime du filtrat.

La culture dissoute par ce procédé devenait elle même capable de dissoudre d'autres cultures, tel le filtrat primitif; ce qui prouvait que le phénomène se répétait en série.

D'Hérèlle crut voir en ce fait une réproduction du virus dans les cultures lysées.

Tous les éssais d'une démonstration microscopique du virus ont échoué et tous les éfforts pour avoir une culture en dehors des bactéries n'ont pas reussi.

Dès lors ce virus présentait quelques propriétés très particulières; quoique il eut une vitalité très rare parmi les êtres de ce groupement, puisqu'il conservait sa virulence dans les filtrats pendant plus d'un an; malgré sa résistance très grande envers les agents physiques, puisque la chaleur qui tue les bactéries parasitées est insuffisante à le détruire, malgré sa résistance toute spéciale aux antiseptiques; malgré tout ça, ce virus filtrant ne se réproduit que très difficilement. Il suffit de tuer les bactéries par un procédé quelconque pour que la culture du virus devienne impossible. Méme si l'on mantient les bactéries vivantes dans les cultures, on remarque que le bactériophage

adapté au b. SHIGA, présente une certaine difficulté á se multiplier dans les cultures du b. FLEXNER.

Le bactériophage de d'Hérèlle possède donc une sensibilité envers le moindre changement du milieu selon la spécificité des germes, qui n'est guère comparable qu'à celle des anticorps.

L'éxamen de ces faits et d'autres semblables, ont induit Kabeshima á considérer le virus comme un ferment d'immunité produit par les germes ou bien une prodiastase, capable d'étre activée par une kinase de l'intestin laquelle agirait mème en des dilutions fort étendues. Cependant on remarquât qu'après une dilution énorme, par des passages succéssives, le phénomène ne s'afaiblissait point, ce qui s'opposait à l'idée d'une kinase telle que Kabeshima l'avait supposée.

Bordet émit une opinion qui jusqu'à présent nous semble la plus acceptable. Il considère le bactériophage un ferment sécrété par les germes en conséquence de la réaction exercée sur eux, par les organismes en état d'immunité. Bordet a basé son hypothèse sur des expériences très intéréssantes qui ont raproché le phénomène de la lyse en série des procédés de l'immunité. Ayant vacciné des cobayes contre le bacille Coli il parvint à retirer de l'exudat péritoneal de ces animaux, un agent lytique avec des propriétés tout á fait semblables au virus de d'Hérèlle.

Il arrive souvent que les cultures traitées par le bactériophage ne sont pas complètement lysées. En ces conditions quelque temps après on remarque la prolifération de nouveaux germes lesquels peuvent être lysés à leur tour comme les autres. Il est important de retenir que ces phénomènes de lyse et prolifération sont alternants. Bordet croit que le ferment provient de ces germes qui ont résisté á l'action du bactériophage. Un fait s'oppose cependant á cett'opinion. Si l'on considère les germes non lysés comme les agents indirects du phénomène bartériophagique, la quantité du ferment produit, devrait étre jusqu'à un certain point, proportionelle à la quantité de germes proliférés en présence du virus Mais il se passe justement le contraire: la quantité du bactériophage est proportionelle aux germes détruits par la lyse et les cultures les moins lysées sont précisément celles dont les filtrats présentent une plus petite quantité de ferment. Tout se passe donc selon l'opinion de d'Hérèlle, c'est à-dire, comme si l'agent producteur de la lyse se réproduisit dans le cellules attaquées.

Tout dernièrement Bail, a construit une hypothèse assez hasardeuse: basé sur la production du bactériophage aux dépens des bactéries lysées, il le considère comme une forme filtrante du bacille détruit. Sous cette nouvelle forme le germe aurait besoin pour sa nutrition, de la matière même des bactéries vivantes.

Non obstant, la plupart des auteurs modernes, surtout français, se rallient á l'opinion de d'Hérèlle, presque sans réserves.

L'année dernière il nous a été donné de rechercher huit fois, sur des matières fécales de plusieurs malades de le H. N. de Alienados do Rio de Janeiro, le bactériophage de d'Hérèlle et sept fois nous l'avons constaté. Une fois la lyse s'est produite en 48 heures; les autres fois au bout de huit jours, l'agent lytique s'étant présenté néttement à la seconde passage.

Chez des individus considérés comme sains le résultat ètait tantôt positif tantôt negatif. Parfois les résultats variaient selon le moment de l'émission des matières: dans un cas éxaminé cinq fois le bactériophage pour le b. SHIGA se présenta trois fois.

Chez d'autres individus sains les résultats négatifs ont été constants, même aprés des purgatifs salins. Un de ces individus quelque temps après fit una infection typhique et le 18º jour de la maladie, nous avons pu constater la présence d'un bactériophage pour le b. d'EBERTH.

Nous avons reussi très facilement à adapter au b. FLEXNER et Y, le bactériophage SHIGA isolé tout au commencement de nos recherches et dont nous nous sommes

servis après pour nos études. Nous l'avons employé sur des échantillons du b. typhique N° 1 et même après un travail pénible de plusieurs passages nous n'avons pas reussi à avoir la lyse complète de cette souche.

Les filtrats obtenus de cette lyse partielle agissaient cependant très bien sur l'échantillon N° 18 et présentaient une action graduellement moins forte sur une série d'échantillons. Ces passages réglés par la sensibilité spéciale à chaque échantillon ont fourni un bactériophage qui lysait complètement le b. typhique n° 1.

Nous avons obtenu plusieurs fois des bactériophages originaux sans laisser les matières 24 heures à l'étuve.

Chez un individu supposé normal, dont les fèces fournissaient parfois du bactériophage, il a été possible d'isoler celui-ci toutes les fois qu'il se présentait dans les 24 heures, et pour cela il suffisait de dissoudre les matières dans du bouillon et de les filtrer.

La bactériolyse se produit quoique faiblement dans les milieux privés d'albumine et contenant seulement des sels d'acides aminés (aspartate et glicocolate de sodium). La lyse se rattache étroitemeut à l'activité vitale des bactéries et se fait proportionellement á son activité. Plus la prolifération d'un germe dans un milieu de culture est nombreuse, plus l'activité lytique du filtrat de cette culture devient grande.

Dans l'eau physiologique, en apparence il n'y a pas de lyse, mais cependant elle se produit quoique très difficilement, car si l'on dóse le pouvoir anticomplémentaire d'une émulsion de germes et si l'on ajoute quelques gouttes de bactériophage, ce pouvoir baisse franchement.

Les bactériophages jouissent des propriétés des extraits des germes respectifs, ils fixent le complement et épuisent les agglutinines. Les rapports entre le bactériophage et les germes de ce groupe ne sont pas analogues aux rapports que ces germes mantiennent avec l'agglutination.

Gratia a prouvé que la réaction du milieu exerce une influence considérable sur le phénomène lytique, et a constaté que cette action ne s'éxerce qu'entre ph-7,2 et 8,5. Dans nos recherches nous avons jugé l'activité du bactériophage par son pouvoir d'inhibition sur la prolifération des germes et nous avons pu constater que le bactériophage éxerce encore ce pouvoir à une concentration de ph-5,1, réaction franchement acide au tournesol. (Ce qui est contraire aux données de d'Hérèlle), à laquelle végete encore le b. FLEXNER. La réaction du milieu doit éxercer sur la lyse une influence indirecte dûe à l'action nocive qu'elle aurait sur l'activité vitale de la bactérie. Le degré d'acidité capable d'empêcher la bactériolyse, ne doit donc être identique pour tous les germes.

En ensemençant des échantillons sensibles même dans les bactériophages les plus actifs, nous avons pu obtenir des races résistentes à la bactériolyse. Ces races isolées en culture pure ne présentaient de capsules telles que d'Hérèlle les a décriptes. En bouillon on obtient des cultures de germes agglutinés en amas très fins qui deviennent plus grossiers si l'on y ajoute de nouveau quelques gouttes de bactériophage. Nous croyons que les capsules des bactéries en contact avec le bactériophage n'indiquent pas une plus grande résistance envers le virus; elles réprésent plutôt un degré initial de la lyse et on peut les voir dans les cultures sur milieux solides peu de temps après l'addition du bactériophage. Plus tard on trouvera les germes dilatés et la substance colorable distribuée d'une façon homogène (formes en levure). La lyse se produit alors par éclatement du germe.

Les bactéries tuées même que ce soit par le formol ne sont pas lysables par le bactériophage; cependant les émulsions de bactéries mortes adsorbent le bactériohpage d'une façon spécifique.

Experience: Une boite de Roux a été ensemencée avec le b. FLEXNER (culture de 24 heures à 37°) ensuite emulsionée en 25 cc. de boullion Martin et soumise à la

emperature de 60° pendant une heure afin de tuer les germes. Après refroidissement on a ajouté 5 gouttes de bactériophage FLEXNER et le tout fût maintenu pendant 24 heures à 37°. Puis on a filtré en bougie. Le filtrat étant dilué à 1/10.000, semblait ne plus empêcher la prolifération du b. FLEXNER. Une émulsion de *Staphylococcus aureus* soumise au même traitement nous a fourni un filtrat qui semblait ne pas empêcher la germination du b. FLEXNER, dilué à 1/10.000.000. On a laissé plus de deux jours à la température de la chambre les tubes contenant les dilutions des filtrats, et qui présentaient tous des cultures du b. FLEXNER. Ensuite on les chauffa pendant une heure à 58° et on constata la présence du bactériophage à tous. Ces résultats sont d'accord précisément avec les données qui nous avaient fourni notre première lecture de l'expérience. La dilution (10^{-8}) du tube dans lequel le bactériophage du filtrat de *Staphylococcus* avait empêché la lyse est à peu près celle qu'éxige le bactériophage tout pur. (10^{-9}). Si l'on déduit la quantité de bactériophage adsorbé par la bougie, on vérifie que l'adsortion de celui-ci par le *Staphylococcus* est presque nulle. L'adsortion par les germes homologues est 1000 fois plus grande.

On doit employer en ces dosages une pipète stérilisée pour chaque tube de dilution car le bactériophage reste adhérent au verre tel un colorant et la petite quantité qui se détache et passe dans le liquide est suffisante pour empêcher le dévéllopement de la culture. Avec la même pipète ayant pour commencer 1 cc. de bactériophage on parvient à empêcher la culture en plus d'une vingtaine de tubes.

Dans une note écrite en collaboration avec MACHADO et publiée dans le "Brazil-Medico" nous avons tenu à insister sur l'influence des serums spécifiques antimicrobiens sur le phénomène de la lyse. Nous avons établi d'une façon irréfutable que ces serums empêchent completement le procédé lityque tout à fait comme font les serums antibactériophagiques et cependant il nous a été impossible d'obtenir un bactériophage de contamination sur les cultures avec lesquelles avaient été inoculés les animaux qui fournirent les serums. Voici le tableau où ces résultats ont été résumés:

En une série de tubes de bouillon MARTIN (10 cc. à peu près) nous avons mis des quantités décrescentes de serum SHIGA agglutinant jusqu'à 1/5000 et une quantité fixe de bactériophage. Après une heure de contact à 37° (ce dont on pourrait se passer) nous avons ensemencé tous les tubes avec la même quantité de b. SHIGA.

	Serum Shiga	Bact. Shiga	Bacillus Shiga	Résultat avec 24 h. à 37°
1° tube	10 gouttes	16 gouttes	3 gouttes	Culture agglutinée
				Come au tube n° 7.
2° «	5			Depôt moindre aggl.
3° «	1			Depôt insignifiant.
4° «	10 g. dil. 1/10	« « «	« « «	Depôt imperceptible.
5° «	5			Idem, idem.
6° «	1			Idem, idem.
7° «	10 gouttes	——		Fort depôt agglutiné.
8° «	——	16 gouttes		Tube limpide.
9° «	10 gouttes	——	——	Idem, idem.
10°	——	16 gouttes	——	Idem, idem.
11° «	——	——	3 gouttes	Trouble.

En cet article nous ajoutions que l'action du sérum était *spécifique* (1) et qu'on trouvait une action identique au serum de convalescents de fiévre typhoide envers le bactériophage typhique.

Une analyse plus détaillée du phénomène nous a mené a la conclusion que le serum n'agit pas directement en neutralisant le bactériophage mais qu'il se borne à protéger les germes contre l'action lytique tel les serums anti-bactériophagiques de d'Hérèlle.

(1) Les bactériophages que nous avons employé dans ces expériences avaient été spécifiés par plus de 8 passages successives.

Par des dosages successiyes nous avons pu déterminer que trois gouttes de notre serum SHIGA étaient capables de neutraliser environ 3 cc. de bactériophage actif. (1/20). Nous avons additionné 16 gouttes de bactériophage à 3 cc. de serum SHIGA et après un contact de 24 heures à 37° ayant dilué le tout en bouillon MARTIN (10 cc,) nous l'avons transporté dans un ballon de bouillon contenant 200 cc. à peu près. Par suite tous les jours nous ajoutions une émulsion de b. SHIGA équivalente à une culture de gélose de 24 heures. Après l'épuisement des anticorps c'est à dire au bout de 4 jours nous avons filtré la culture totale et le filtrat avait des propriétés lytiques qui se répétaient en série tel un vrai bactériophage. Dans une autre proportion de serum et bactériophage (3 gouttes de serum et 16 gouttes de bactériophage) les faits restent les mêmes et nous croyons pouvoir conclure par là que le bactériophage n'est pas détruit directement par le serum. S'il en est comme ça, il semble, que l'action du serum dans ce phénomène doit s'éxercer sur les bactéries. Pour le verifier nous avons procédé à l'experience suivante: On a ajouté 1 cc. de serum SHIGA à 10 cc. de bouillon et on a ensemencé 3 gouttes d'une èmulsion de culture jeunne de b. SHIGA en gélose. Le lendemain les germes proliférés et aggluttinés ont été lavés trois fois en bouillon, qui fut remplacé presque complètement par le bactériophage SHIGA. Au bout de 48 heures, persistait encore un grand depôt de germes aggluttinés.

L'aggluttination ayant pu rétrecir la surface d'ataque des bactéries, nous l'avons consideré comme une cause possible d'erreur à l'interprétation des résultats.

En admettant que l'action du serum s'éxerçât exclusivement par protection aux germes et restât tout a fait indépendente du bactériophage, il serait évident qu'une même quantité de germes devrait proliférer dans une quantité donnée de serum, sans que la quantité de bactériophage ajoutée pût éxercer quelque influence.

Ce n'est pas ce qu'on constate, tel nous prouve le tableau ci-dessous.

	Bact. Shiga	Extrait Shiga	Bouillon Martin	Serum Shiga	Bacillus Shiga	Lecture avec 24 heures à 37°
1° tube	5 cc.	— — —	— — —	3 gouttes	3 gouttes	Flocons sans germes
2° «	10 gouttes	5 cc.	— — —	«	«	
3° «	« «	— — —	5 cc.	«	«	Germes aggluttinée
4° «	4 cc.	— — —	— — —	«	«	Flocons sans germes
5° «	3 cc.	— — —	— — —		«	Flocons avec quelques germes
6° «	2 cc.	— — —	— — —	«	«	Germes aggluttinés
7° «	1 cc.	— — —	— — —	«	«	
8° «	10 gouttes	— — —	— — —			
9° «	1 goutte	— — —	— — —			
10° «	— — —	— — —	— — —	«	«	«
11° «	10 gouttes	— — —	— — —	«	«	Limpide
12° «	1 goutte	— — —	— — —	«	«	
13° «	10 gouttes	— — —	— — —	3 gouttes	«	«
14° «	— — —	— — —	— — —	— — —	3 gouttes	Trouble

Il est aisé de voir que 4 cc. de bactériophage SHIGA ont le pouvoir d'empêcher complètement le dévéllopement de la culture si l'on additionne 3 gouttes de serum SHIGA. Si nous considerons maintenant les tubes témoins du tube nº 1, on vérifie qu'au tube nº 3 la dilution n'éxerce aucune influence sur la lyse. Le tube nº 2 nous montre un fait plus curieux: 10 gouttes de bactériophage agissent en présence de trois gouttes de serum si l'on y ajoute une quantité suffisante de l'extrait SHIGA (c'est à dire d'un filtrat d'une culture pure du b. SHIGA, ayant végété huit jours à 37º).

Pour interpréter ces faits il faut admettre selon notre opinion que les différents anticorps d'un même germe soient attachés à une fraction donnée de globuline. Cette globuline ayant été precipitée dans les tubes en question a attiré avec elle les anticorps dont elle était le subsctractum albuminoide.

Cette action des extraits sur le pouvoir antilytique des serums spécifiques, va nous servir maintenant á prouver que le bactériophage n'est pas neutralisé diréctement par le serum.

Nous avons ajouté, 3 gouttes de serum SHIGA et 10 gouttes de bactériophage SHIGA à 10 cc. de bouillon MARTIN. Après trois heures à l'étuve à 37º nous avons additionné 5 cc. d'extrait SHIGA et ensuite, le tout a été ensemencé avec trois gouttes d'une émulsion de b. SHIGA. A coté nous avons placé les témoins nécéssaires au contrôle de l'experience. Au bout de 24 heures nous avons constaté qu'aucune prolifération de germes ne s'était passé, c'est à dire que le bactériophage malgré le long contact avec le serum n'a pas perdu sa capacité lytique.

On pourrait supposer que le serum exerçât sur le bactériophage une action précipitante et que l'extrait du germe, fût capable de dissoudre ce précipité qui serait peut-être imperceptible à l'oeil. Mais ce n'est pas le cas, tel nous montre l'expérience sinvante: Nous avons mélangé dans les trois tubes de bouillon MARTIN (10 cc. chacun) trois gouttes de serum et 10 gouttes de bactériophage homologue. Au bout de 24 h. à l'étuve à 37º nous avons filtré en bougie le liquide et, après, nous avons ajouté 5 cc. de l'extrait respectif, au filtrat, et au tube 2º. Ensuite on a ensemencé les trois tubes avec le germe spécifique (b. SHIGA). On les laissa encore 24 heures à l'étuve à 37º; les deux prémiers tubes sont restés clairs, limpides, le troisième présentait un depôt de germes agglutinés.

Le pouvoir d'empêcher la lyse, exercé par les serums spécifiques, agit donc sans aucun doute sur les germes et son action est due à des anticorps. Dans ces conditions elle ne peut être expliquée que par un phénomène de blocus.

Il est aisé de voir que l'agglutination n'intervient pas dans le phénomène car le serum SHIGA par exemple (même employé en dilution fortement agglutinante envers les b. SHIGA ou FLEXNER) ne protège point ces germes contre les respectifs bactériophages. D'un autre coté on ne saurait attribuer aux précipitines un rôle quelconque dans le phénomène si l'on pense au titre de la dilution à laquelle le serum empêche la lyse.

Une étude plus longue pourra nous renseigner si ce sont les ambocepteurs les responsables pour le phénomène.

Ce que l'on peut, à notre avis, conclure des lors, ce qui a une grande importance au point de vue de l'immunité, *c'est que le bactériophage se colle au germe par le même procédé d'adsortion spécifique dont le germe se sert pour fixer l'anticorps; ou alors ce qui revient au même, il existe un anticorps identique au bactériophage par son groupement cytophile*, pour employer le langage d'Ehrlich. Comme il a été dit au commencement, les faits que nous venons de rapporter ont trait à des serums obtenus de convalescents d'infection naturelle ou bien des animaux immunisés avec des cultures vivantes de bactéries.

Si l'on voulait à tout prix faire subsister l'opinion de d'Hérelle, on pourrait admettre aussi bien dans la vaccination artificielle comme dans l'infection naturelle que

la pénétration des bacteries vivantes dans l'économie des organismes pourrait créer un bon milieu de culture au bactériophage qu'existerait par hasard quelque part dans ces mêmes organismes, Ce bacteriophage ainsi cultivé se répandrait alors et produirait dans les serums respectifs des propriétés anti-bactériophagiques.

Cette hypothese devient insoutenable devant la considération que les serums des animaux (chiens) inoculés a plusieurs reprises avec des bactéries mortes présentent des propriétés anti-lytiques spécifiques aussi grandes que celles des serums que nous avons rapporté en détail. Nous pensons que les serums anti-bactériophagiques ne different guère des serums anti-infectieux mais nous ne sommes à même de l'assurer d'une façon préremptoire parce qu'il nous manquait assez de serum pour un examen complet. Nous avons préféré en en ces conditions employer plutôt ce qui nous restait pour étudier d'autres aspects du problème.

(Néanmoins nous pouvons dès à présent assurer que les simples extraits du b. Flexner neutralisent parfaitement les propriétés anti-lytiques des serums. anti-bactériophagiques Flexner. Cela veut dire que aussi dans ces serums ce n'est pas un anticorps spécial à un virus qui détermine l'inhibition de la lyse, mais un anticorps formé contre des antigènes du bacille dissous dans le bouillon par le procédé lytique.)

Étant donnée la ressemblance entre les serums spécifiques pour les germes et les serums anti-bactériophagiques nous avons éssayé de voir comment les choses se passaient pour la fixation du complément en présence de bactériophages hétérologues (1).

On voit par lá que, en admettant que ces serums soient anti-bactériophagiques, le bactériophage ne fixerait le complément qu'en présence des serums homologues. Ça n'est pas ce qu'assure d'Hérèlle.

Cet auteur et Eliava ont affirmé que n'importe quel bactériophage serait capable de fixer le complément en présence d'un serum anti-bactériophagique, fût il obtenu de n'importe quel animal. Ainsi, ces auteurs ont obtenu la fixation du complément en présence de serum anti-bactériophagique Shiga avec du bactériophage Shiga, mais aussi avec du bactériophage pour la peste qu'il ait été isolé de convalescents de cette maladie ou qu'il ait été trouvé dans les excréments de rats capturés dans des endroits où la peste reste endémique.

(1) Voir le tableau ci-joint.

Fixation du complement

Bact. Shiga	Serum Shiga	Serum Flexner	Pesteux Serum	Résultat
0,5	0,1	——	——	++++
0,5	0,05	——	——	++++
0,5	0,025	——	——	++++
«	0,01	——	——	h. total
	——	0,1	——	«
	——	0,05	——	«
«	——	0,025	——	«
«	——	0,01	——	«
	——	——	0,1	++
«	——	——	0,05	h. total
«	——	——	0,25	«

Bact. Flexner	Serum Shiga	Serum Flexner	Serum Pestoso	Résultat
0,5	0,1	——	——	++
0,5	0,05	——	——	h. total
0,5	0,025	——	——	« «
0,5	——	0,1	——	++++
«	——	0,05	——	+++
«	——	0,025	——	h. total
«	——	——	0,1	++
«	——	——	0,05	h. total
——	0,1	——	——	« «
——	——	0,1		« «
——	——	——	0,1	++
——	——	——	0,05	h. total

A notre avis cette assértion réprésente l'argument le plus fort qu'on a apporté jusqu'à présent en appui de l'hypothèse de d'Hérèlle, il nous semble tellement décisif que nous ne concevons pas qu'on puisse admettre d'autre opinion sur la nature du bactériophage. Voici le résultat de nos expériences visant éclaircir ce point:

Serum anti-bactériophagique Flexner: nous l'avons obtenu par inoculation d'un lapin tous les 7 jours avec 2, 4, 8, 10 cc. d'un bactériophage Flexner fortement actif, et saignant l'animal 12 jours après la dernière inoculation. Le serum obtenu fut inactivé pendant 1/2 heure à 56°. Il agit en empêchant spécifiquement la lyse.

Bactériophage Flexner: Ayant été dilué jusqu'à environ 10^{-10} empêche complètement le dévéllopement de trois gouttes de b. Flexner en émulsion (culture de gélose de 24 heures en 10 cc. de bouillon Martin).

Bactériophage Shiga: Ayant été dilué á 10^{-10} empêche comme le bactériophage Flexner ci dessus le dévéllopement du b. Shiga.

Extrait Flexner: C'est le filtrat d'une culture b. Flexner mantenue à l'étuve à 37° pendant huit jours.

Extrait Shiga: C'est le filtrat d'une culture de b. Shiga mantenue à l'étuve à 37° pendant huit jours.

Bouillon Martin (du même stock qui fût utilisé pour la préparation des bactériophages et des extraits): obtenu selon la technique habituelle en laissant la fermentation se passer pendant 24 h. à 50° en présence d'acide chlorhydrique à 10°/oo.

Réaction de fixation

On employa aussi bien les antigènes (bactériophages et extraits) comme le bouillon Martin, à la dose de 0,5 moitié de la dose non empêchante.

La fixation se fit pendant une heure a 37°. La lecture de l'hémolyse au bout d'une heure à 37°.

Serum anti bactériophage Flexner

	0,5	0,25	0,1	0,05	0,025
Bact. Shiga	++++	++++	+++	h. total	h. total
» Flexner	++ ++	++++	++++	++++	++
Extrait Shiga	++++	++++	+++	h. total	h. total
Flexner	++++	++++	++++	+++	+++
Bouillon Martin	++++	++++	+++	h. total	h. total
Eau physiologique	h. total	h. total	h. total	h. total	h. total

Voici une réaction executée simultanément où on employa le serum Flexner au lieu du serum antibactériophagique.

Serum Flexner

	0,1	0,05	0,025	0,01
Bact. Shiga	++	h. total	h. total	h. total
» Flexner	++++	++++	+++	h. total
Extrait Shiga	++	h. total	h. total	h. total
Flexner	++++	++++	++	++

On constate par conséquence que malgré la grande activité de nos bactériophages les extraits des germes respectifs n'en fixent pas moins le complément, aussi bien en présence de serum Flexner qu'en présence du serum anti bactériophagique.

Les résultats obtenus par d'Hérèlle ne peuvent être expliqués que par une fixation alléatoire due à des substances du bouillon qui garderaient encore des propriétés antigéniques conservées par une digestion pepsique incomplète.

On ne peut pas attribuer raisonablement au bactériophage des propriétés antigéniques ni par la fixation du compiément ni par l'étude de l'action anti-lytique des serums spécifiques. Cela fait penser qu'à la bactériolyse en série il ne s'agit pas d'un être vivant.

L'étude du bactériophage devient particulièrement intéressant car il semble montrer que l'ancienne théorie de Buchner dévéllopée dernièrement par Herzfeld et Klinger selon laquelle l'anticorps viendrait de l'antigène n'était pas tellement inéxacte comme ont fait croire les travaux de plusieurs auteurs et surtout ceux de Knorr, Roux et Madsen.

Nous croyons que le bactériophage soit un ferment ou plutôt un catalyseur appartenant au germe et employé par lui en son métabolisme normal pour la désintégration de certaines substances composantes de la membrane. Un procédé digestif spécial semblable à ceux qui se passent dans l'intestin ou dans le milieu interne quand l'antigène est introduit par voie parentérale met en liberté le catalyseur en question. Celui-ci, une fois rompu l'équilibre qui l'assujétit dans la cellule vivante agit sur les germes en détruisant les parties de la membrane que lui sont respectives et en produisant en consequence un deséquilibre osmotique. Ce changement des conditions d'osmose dans la cellule determine une hydratation desordonnée et ensuite l'éclatement de la cellule qui répand dans le milieu une certaine quantité de catalyseur. L'essence même du procédé ne peut naturellement être expliquée que par des conjectures.

Le catalyseur doit être un colloide parce que le bactériophage n'est pas dialisable malgrè la relative simplicité de sa composition chimique comme semble attester le défaut de propriétes antigéniques. La faculté de s'attacher aux germes morts, sans les lyser fait croire qu'une substance labile de la bactérie joue un certain rôle dans le phénomène. Ce serait une sorte de endo-complément non sécrétable.

Il nous semble hors de doute que l'action s'éxerce sur la membrane étant donné l'aspect de troubles osmotiques qui présentent les bactéries atteintes par le bactériophage. Nous envisageons donc le bactériophage comme une *phase* des plus importantes du procédé de vaccination anti-microbienne au lieu de le considérer comme un état d'immunité. Il s'agirait de la phase initiale de la désintégration de l'antigène qu'il ait été introduit par voie intestinale ou bien par voie parenterale. Dans ce dernier cas le bactériophage ayant atteint une simplicité encore plus grande entrerait, comme les autres catalyseurs de l'antigène dans la cellule en qualité d'aliment. Lá il serait incorporé par le travail cellulaire á une pseudo-globuline qui ne serait autre chose qu'un anticorps.

Le passage de ces catalyseurs modifiés de la sort dans le plasma, dû à une sécrétion ou excrétion cellulaire produit l'immunité humorale; la rétention de quelques petites quantités dans l'intérieur de certaines cellules pendant un temps indéterminé explique l'immunité cellulaire.

De cette conception nait immediatement une conclusion qui peut être soumise á l'expérience.

En admettant que les groupements cytophiles des anticorps soient des catalyseurs non antigéniques, il ne doit pas exister des anti-anticorps dans le vrai sens du mot, c'est à dire des anticorps capables de saturer spécifiquement le groupement spécifique d'autres anticorps. Quoique les opinions ne soient pas unanimes, à ce sujet nous ne croyons pas qu'on ait pu démontrer par l'expérience l'éxistence d'anticorps pour des anticorps; mais au contraire les travaux que nous connaissons sur cette question sont tous négatifs.

Si l'on vaccine un lapin avec du serum de cheval fortement antitoxique, on remarque quele serum de lapin dévient capable de

neutraliser l'antitoxine du cheval mais n'exerce point la même action vis à vis l'antitoxine de chèvre ou de boeuf.

Dehne et Hamburger dans uns travail remarquable que nous avons répété avec pleine confirmation, ont démontré en toute évidence qu'il s'agit lá tout bonnement d'une précipitation, c'est á dire que la partie antigénique de l'anticorps est exclusivement le substractum albuminoide qui contient la partie spécifique.

L'antitoxine traitée par la pseudo-anti-antitoxine se précipite mais peut se régénérer par dissolution du précipité en serum normal de cheval. D'un autre coté on obtient la même anti-antitoxine en inoculant des lapins avec du serum normal d'animaux de la même espèce de ceux qui ont fourni l'antitoxine, c'est à dire tout simplement avec des serums précipitants.

La précipitation de l'antitoxine est un procédé absolument spécifique en tant que concerne á l'espèce animal d'où provient l'antitoxine.

Fonteyne a voulu vérifier si par hasard en cette neutralisation existait une vraie anti-antitoxine masquée par la précipitation.

Il essaya alors de vacciner quelques animaux avec des serums riches en antitoxines et provenant d'anlmaux de la même espèce.

Malgré que le groupement spécifique fut parfaitement étranger á ces animau'x leur serum n'a jamais montré les moindres vestiges d'anti-antitoxine.

Kraus et Pribram, v. Eisler et Tsuru ont confirmé presque sans diverger les travaux de Dehne et Hamburger vis à vis d'autres anticorps. L'analyse des travaux éxécutés dans ce sens montre effectivement qu'on n'a jamais réussi à demontrer l'existence de vrais anti-anticorps, c'est à dire, démontrer que le groupement spécifique pour l'antigène de l'anticorps, fut à son tour antigénique.

Si nous admettons par conséquence que la partie spécifique des anticorps soit formée par des catalyseurs de l'antigène, la spécificité perd tout ce qu'elle a de merveilleux et rentre dans le rang vulgaire de nos observations courrentes. *La spécificité dans l'immunité n'est plus une création facile et rapide de l'organisme qui s'immunise lui même mais elle devient l'utilisation d'une spécificite qu'existait déjá dans le germe et qu'il a acquis comme tous les autres êtres vivants en une longue et pénible évolution.*

Un anticorps diffère donc du bactériophage exclusivement par la structure de son substractum albuminoide. Ce substractum est d'ailleurs la seule différence qu'existe entre deux anticorps d'un même antigène provenants d'animaux d'éspèce différente.

Cette hypothèse nous permet d'interpréter certains faits particuliers. On sait que l'introduction des antigènes les plus différents par voie orale ne détermine que très rarement une immunité valable, ce qui nous prouve que, malgré la digestion, la partie utile de l'antigène n'est pas absorbée. Ce fait s'accorde avec l'élimination de certains catalyseurs par les fèces tel succede avec le bactériophage. Il nous semble que l'apparition du bactériophage coincide avec le passage par l'intestin gréle. Nous avons nourri des lapins avec des émulsion du b. Flexner, tués préalablement par ia chaleur (60° pendant une heure). On leur fournissait un tube de gélose par jour. Au bout du 7° jour le filtrat des matières (pâteuses) ceuillies dans le caecum a fourni un bactériophage très actif.

Cette interprétation pourrait expliquer la présence intermitente du bactériophage dans les selles de certains individus d'aspect normal.

Celui que nous avons examiné était justement un constipé habituel; dans ses urines nous avons trouvé souvent l'indol, ce qui prouve que son intestin gréle était parfois contaminé par la flore du gros intestin.

Mais un fait attire, surtout, la curiosité par son allure paradoxale, c'est ce que l'on nomme le phénomène des ondes, duquel nous avons déjà parlé tout à l'heure. Ce phénomène décript la première fois par

Gratia et confirmé par plusieurs auteurs consiste en des proliférations alternantes. Si l'on additionne à une culture adulte une quantité suffisante de bactériophage on obtient en quelques heures la lyse. La culture devient limpide mais la lyse n'est pas définitive et dans un temps plus ou moins long un trouble léger apparait; puis disparait, pour réparaitre et de noveau disparaitre et ainsi de suite.

D'Hérèlle explique ce phénomène en admettant que les bactéries en contact avec leur virus infectieux sont vaccinées et acquièrent un état d'immunité semblable à celui des organismes supérieurs envers les bactéries. Cet état d'immunité serait soumis à des oscillations provoquées par des changements *inexplicables* de la virulence du bactériophage. Cette hypothèse n'est pas faite pour donner pleine satisfaction. D'abord parce que le phénomène se répète à des intervalles réguliers, ensuite parce que les bactéries lysées après avoir végété en présence du bactériophage ont gardé toujours contact avec le virus vaccinant.

Notre hypothèse, au contraire, permet d'interpreter d'une manière satisfaisante ce phénomène resté jusqu'ici inexplicable

On sait que tous les anticorps additionnés en excès à l'antigène ne l'impressionnent pas; c'est ce que l'on appelle déviation du complément pour les sensibilisatrices ou bien ce que l'on nomme pour les agglutinines et les précipitines zone des agglutinoides et précipitinoides. La réaction antigéne-anticorps ne se réalise que lorsque les deux sont en des proportions qui ne dépassen pas certaines limites (1). C'est ce qui arrive surement avec le bactériophage. Quand ou ajoute à la culture adulte d'un germe une goutte du respectif bactériophage la lyse a lieu et pendant que la concentration de bactériophage s'accroit, selon notre hypothese, le nombre des germes vivants diminue progressivement. A un certain moment la quantité de bactériophage en rapport au nombre des germes devient tellement excessive que la réaction s'arrète. Les germes non encore aiteints peuvent se réproduirent sans etre lysés par le ferment, mais lorsque leur nombre devient assez grand pour rétablir les conditions d'une nouvelle lyse, celle ci se produit et ainsi de suite.

Ce phénomène ne doit pas etre confondu avec celui de la formation de bactéries resistentes à la lyse, provenantes de la prolifération définitive en présence du bactériophage.

L'isolement en plaque permet alors d'obtenir des cultures qui durant quelques répiquages fournissent des bactéries insensibles au bactériophage. Ce fait d'observation fut le point de départ où d'Hérèlle s'est appuié pour admetre que les bactéries se vaccinent contre le virus.

Ayant remarqué que le virus peut être détruit par les sels de quinine (Eliava et Pozersky); comme d'ailleurs il arrive aux serum-lipazes (Peter et Reinicke) – d'Hérèlle s'est demandé si par hasard il ne s'agirait pas d'un protozoaire.

En rapport avec cette idée il convient de rappeler que jusqu'à présent on ne connait pas chez les êtres unicellulaires aussi simples que les bactéries aucun phénomène de résistance acquise contre le parasitisme de protozoaires. Les hématies que l'on a souvent comparé aux bactéries (ce qui se justifie pleinement du point de vue de l'immunité) n'acquièrent pas non plus une résistance envers le paludisme la piroplasmose etc. et lorsque se trouvent, en présence de ces hematozoaires, deviennent inévitablement leur proie. Les réinfections surtout dans le cas du paludisme sont toujours possibles même chez les individus qui ont été longtemps parasités.

Il arrive tout autrement lorsqu'on envisage les poisons. Là nous avons des exemples très nets qui se rapprochent beaucoup à notre avis de la formation de races resistentes au bactériophage.

Camus et Gley ont vacciné des lapins

(1)—Bordet vient de montrer que l'on verifie aussi l'inhibition de la lyse si l'on employe un excès de bactéries. L'analogie entre ces phénomènes devient encore plus frappante.

contre le serum d'anguille qui est fortement hemolytique pour les hématies de ces animaux; ils ont constaté au bout d'un certain temps que les serums des lapins contenaient une antitoxine spécifique. Et plus encore ils ont verifié que les globules rouges, eux-mêmes, séparés du serum et lavés afin d'écarter les anticorps, êtaient insensibles au serum d'anguille.

L'observation de cette immunité cellulaire nous montre qu'elle n'est pas absolument concomitante à l'immunité humorale antitoxique. Au contraire l'immunité cytologique ne s'établit que peut avant que la quantité des anticorps dans le serum ne commence à baisser, quoique cependant elle n'arrive jamais à remplacer complétement l'immunité humorale.

Selon la doctrine d'Ehrlich, les antitoxines identiques par leur récepteur toxophore aux récepteurs des globules rouges fixeraient les aliments intermediaires (Zwischenprodukten).

A ces aliments sont justement destinés les récepteurs cellulaires. Cette déviation nutritive nuit les globules qui ne pouvant plus se servir de leurs récepteurs les abandonnent.

D'après notre hypothèse le phénomène s'expliquerait encore plus facilement, car l'atitoxine ayant le même groupement cytophile de la toxine, les réceptenrs ne seraient pas abandonnés, mas simplement saturés par l'antitoxine, qui empêcherait forcèment la fixation ultérieur de la toxine. C'est ce que nous croyons se passe envers les bactéries résistentes au bactériophage. En ce dernier cas les récepteurs sont détruits par l'action du bactériophage qui les sature et la perte de ces récepteurs dévient un caracter acquis transmissible naturellement selon les lois de l'hérédité.

Tout dernièrement Watanabe a rappelé que l'on peut isoler par dilutions successives de bactériophage (tel d'Hérèlle l'avait déjà-faitl) des points de lyse très nets, dans les plaques semées avec des bactéries sensibles. Et basé sur ces faits, il s'est permit de concure que ces points ne peuvent être expliqués que si l'on admet la nature vivante du bactériophage c'est à dire en admettant la pullulation *in loco* du bactériophage.

Mais remarquons que le bactériophage est un colloïde et non pas une vraie solution, quil est capable de dètruire les bactéries dans des conditions convenables et de répandre davantage à leurs dépens dans le milieu, la substance lytique. Il devient donc évident qu'au point de la plaque ou tombe une particule colloidale une zone de lyse indépendante se constitue. Et pour bien compendre ce fait il ne nous semble point nécessaire de faire appel à la pullulation d'un être vivant.

Il n'y a pas longtemps Landsteiner ayant vacciné des animaux avec des azoproteines vérifia que les anti-serums obtenus réagissaient spécifiquement envers des substances azoiques d'une composition chimique exactement connue. Celles-ci cependant n'ont pas des propriétés antigéniques.

Il y a là encore un fait que notre façon de voir explique aisément. Le lecteur trouvera bien d'autres que nous nous passons de rapporter et qui s'accordent avec notre hypothèse.

Certes nous n'avons point l'idée d'assurer des vérités définitives. Nous pensons cependant que notre façon d'envisager ces pro. blèmes n'est pas une combinaison adroite qui servi rait exclusivement à interpreter certains aspects de la question, non expliqués encore. Elle est plus que cela, le seul lien qui reunnit le phénomène de la lyse en serie à celui de l'immunité humorale. Ce rapprochement semblait jusqu'à présent contradictoire. En outre sans chercher à pénétrer dans l'éssence même des phénomènes physico-chimiques qui constitue ces rèactions, notre hypothèse exprime très nettement en une terminologie connue de tout le monde la façon probable dont les faits se réalisent. Elle fait surtout revenir la spécificité de la vaccination à la seule spécificité qui soit vraie, c'est à dire celle que les êtres vivants acquièrent par évolution devant toutes sortes de vicissitudes du milieu extérieur.

Nous tenons à remercier chaudement nos confères Ms. A. MACHADO, F. CARNEIRO, GODOY et C. WERNECK à qui nous avons eut recours plusieurs fois.

Rio le 30 Mars 1922.

ON THE SACHS-GEORGI TEST

as compared with the Wassermann Test.

A study on 2.000 cases

by

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(Sub-assistant pro tem.)

The formation of a precipitate when the serum of a syphilitic individual is brought into contact with the corresponding antigen was known long ago though not used in current practice.

NEUBAUER and ELIAS, SALOMON, PORGES, MEIER and PORGES and also MICHAELIS observed the formation of a precipitate when syphilitic serum and organic antigen where mixed with lecithin or sodium glycocholate.

JACOBSTHAL noticed flocculation in syphilitic serum, brought in contact with antigen obtained from the liver of a heredo-syphilitic foetus. On this fact he established a new test for the diagnosis of syphilis; yet this phenomenon is not constantly observed, as often sera which give an absolutely positive reaction with the WASSERMANN test, fail to flocculate by the method of JACOBSTHAL. This lack of constancy and the irregularity in the appearance of the precipitate are sufficient to render the method unfit for practical use.

The HERMANN PERUTZ test which next appeared, agrees more perfectly with the WASSERMANN test. The antigen used in this case is altogether artificial being a chemical substance. The main difficulty, in obtaining it in good condition, is due to the nature of the chemical substances used, viz. cholesterin and sodium glycocholate.

MEINICKE observed that both positive and negative sera may flocculate in the presence of a special antigen (though with negative sera a precipitate may be wanting); but whereas in the case of negative sera the precipitate dissolves easily and disappears upon adding a saline solution of titrated concentration, in the case of positive sera the precipitate shows no alteration. In this test the antigen employed is made from bullock-heart in various concentrations.

Of the precipitation tests, rapidly described above, none may be used a-

lone without control by the original WASSERMANN process.

SACHS and GEORGI recently described a process of flocculation which in my opinion, is the best hitherto known, and may substitute the WASSERMANN test, if all the component elements are perfectly known and titrated. The technic is much simpler and the results, when compared with those of the WASSERMANN test, agree very well as shown by all the statistics published up to now.

I shall now proceed to give a more detailed description of the preparation of the reactives and of the technic:

Antigen. The antigen used in the SACHS-GEORGI test is bullock-heart. This should be fresh and only the muscular tissue used, cut into small fragments and triturated in a mortar until it becomes a homogeneous pulp; with this an emulsion is made in absolute alcohol, in the proportion of 1 gramme to 5 cc. It is placed, together with glass beads, in a vial, sealed with paraffin and kept in the incubator for a fortnight during which period it has to be shaken twice daily. Finally it is filtered through filter paper and the extract is ready.

In practice the use of only one extract should be avoided, just as one ought not to use one antigen alone in the WASSERMANN test; it is safer to employ three perfectly titrated and controlled extracts. They may be prepared from different fresh bullock hearts or by mixing pieces of various hearts always using the same method.

The antigen thus obtained constitutes the concentrated solution; for use as a reactive it must be diluted with two parts of absolute alcohol, adding cholesterin and finally diluting with physiological solution in the proportion of 1 to 6. The dilution must be made only when the antigen is about to be used. The concentrated solution should be kept well shut in a cool and dark place.

The antigen used in the SACHS test contains much cholesterin but its proportion varies, as neither the antigenic value of the extract nor of the cholesterin are constant. Hence it is necessary to ascertain the optimum of cholesterin to be added to a certain volume of concentrated solution of antigen after diluting in two parts of absolute alcohol. For this purpose a titration has to be made, so as to ascertain the quantity of cholesterin, which, added to the antigen, will cause it to produce flocculation of a known positive serum and will leave a known negative one unaltered.

For this purpose a centesimal solution of cholesterin should be prepared and kept in a sealed vial.

Titration of antigen.

For titration the following is required:

1.—Concentrated antigen solution.

2.—Absolute alcohol.

3.—1% alcoholic solution of cholesterin.

4.—Known positive sera.

5.—Known negative sera.

A series of 10 test tubes is then placed at hand and 1cc. of the concentrated solution of antigen and 2 cc. of absolute alcohol are mixed in each tube. The alcoholic cholesterin solution is then added, beginning with 0,1 cc. and gradually increasing up to 1 cc. in the last tube. Ten solutions of antigen with augmenting doses of cholesterin are thus obtained. Each tube now contains a different antigen, to be tried with positive and negative sera.

Now we take a new series of ten test tubes in which we dilute each antigen in physiologic solution at 0,85 % in the proportion of 1 to 5. For this purpose 1 cc. of antigen is mixed with 1 cc. of physiologic solution, is well

shaken and finally the remaining 4 cc. are added.

The aqueous solution of all the antigens being ready, there only remains to mix it with the positive and negative sera. The blood sera should be diluted with physiologic solution at 0,85 % in the proportion of 1 to 10. To 1 cc. of these serum dilutions 0,5 cc. antigen is added. The same process is used for all the antigens, mixing them with positive and negative sera.

The tubes are kept in the incubator at 37°C during 24 hours, at the end of which time the results are read. One notes the tube in which flocculation is most intense and then one observes if the negative sera remain unaltered with the same antigen. In that case the right antigen is determined and there only remains to note the titre of cholesterin used.

Titration should be made with many sera, both positive and negative, in order to know the antigen well before it is currently used.

We give a table, by which the technic just described is easily understood. It refers to one extract only and also to one positive and one negative serum. Another table gives the test of antigen with physiologic solution only, for controlling if flocculation without presence of serum occurs.

Any other extract is titrated in the same way. I constantly obtained excellent results by following this technic and have used it in 2000 cases under control by the WASSERMANN test.

Titatrion of Antigen

Tubes	1	2	3	4	5	6	7	8	9	10
Concentrated Antigen extact.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.
Absolute alcohol.	2 cc.	2 cc.	2 cc.	2 cc.	2 cc.	2 cc.	2 cc.	2 cc.	2 cc.	2 cc.
Alcoholic cholesterin solution 1%.	0,1	0,2	0,3	0,4	0,5	0,6	0,7	0,8	0,9	1 cc.
Dilute the contents of each tube with physiologic saline solution at 0,85% in the proportion of 1 to 6.										
Diluted extracts.	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5
Positive serum at 1/10.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.
24 hours in the incubator at 37°C.										
Diluted extracts.	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5
Negative serum at 1/10.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.
24 hours in the incubator at 37°C.										

Saline Sol. at 0,85%	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.	1 cc.
Diluted extracts	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5	0,5

24 hours in the incubator at 37°C.

Technic for the use of the reaction

Having obtained the titrated antigens it is easy to perform the reaction The antigen is prepared by diluting the concentrated solution in two parts of absolute alcohol and adding the quantity of cholesterin determined by titration. The next step is to make the dilution of the antigen in the proportion of 1:6, as explained above. The serum for examination is diluted with ten parts of physiological solution and to 1 cc. of the resulting mixture 0,5 antigen is added. Known positive and negative sera are used as checks and the test is made with all of them. The tubes are kept in the incubator at 37°C. for 20 hours when the results are noted. (The temperature must remain constant.)

In the accompanying table the three extracts and the whole technic are registered.

The best way to read results consists in holding the tube against a dark background, so as to perceive the smallest flocculae.

The results are classified by the more or less intense flocculation using the following signs: +++ when the flocculation is very strong and a deposit of precipitate is formed in the tube; ++ positive with less precipitate: + weakly positive when the precipitate is thin and only perceived against a dark background;—negative when there is no precipitate.

In the statistics published in the portuguese text, page 121 and referring to 2000 sera submitted to Sachs-Georgi and WASSERMANN tests the above mentioned conventional signs are used; furthermore, controls are indicated by the word testemunhos and the reactions carried out with physiological saline liquid by the abbreviation: liq.

The process is the same as for the blood serum and for greater sensibitiveness the liquid may be used pure.

SACHS—GEORGI Test

	Extr. A.	Extr. B.	Extr. C.
Serum to be tested diluted at 1/10	1 cc.	1 cc.	1 cc.
Antigens	0,5	0,5	0,5
Positive serum diluted at 1/10	1 cc.	1 cc.	1 cc.
Antigens	0,5	0,5	0,5
Negative serum diluted at 1/10	1 cc.	1 cc.	1 cc.
Antigens	0,5	0,5	0,5
Saline Sol. at 0,85%.	1 cc.	1 cc.	1 cc.
Antigens	0,5	0,5	0,5

24 hours in the incubator at 37°C.

SYNOPSIS OF STATISTICS

WASSERMANN TEST positive SACHS-GEORGI test positive	684
WASSERMANN test negative SACHS-GEORGI test negative	1,178
WASSERMANN test positive SACHS-GEORGI test negative	74

WASSERMANN test negative
SACHS-GEORGI test positive } 61
Concordant results — 93,1%
Discordant results — 6,9%

Unfortunaly I was not able obtain the clinical diagnostic of the patients, which would have been of great value in the case of discordant results